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PARTIAL GASTRECTOMY FOR ULCER AND POSTOPERATIVE COMPLICATIONS

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PARTIAL gastrectomy has long been accepted by most authorities as the best form of operative treatment for gastric and duodenal ulcers. In recent years the mortality rate has been so greatly reduced that it need no longer be considered a factor in the choice between medical and surgical treatment.

CLINICAL MATERIAL

The material to be presented here from the 4-year period 1946 to 1949 consists of 280 patients with gastroduodenal ulcer in whom partial gastrectomy was performed. Not included are those operated upon for perforating ulcer (48 cases, including 30 resections), those with bleeding ulcers, operated upon as an emergency measure (9 cases), or those with marginal ulcer (6 cases). The 11 cases in which only gastrojejunostomy was performed and the 2 cases in which only vagus resection was done are not included. No selection has been made in the partial gastrectomy material. Patients with penetrating ulcers or protected perforation, bleeding ulcer in which transfusions have brought the blood status back to normal or nearly normal, patients with retention or complicating diseases such as chronic respiratory infections, heart or blood vessel diseases, and so on, are all included.

Of a total of 280 patients treated by partial gastrectomy, 65 had gastric ulcer, 8 had ulcers of stomach and duodenum, and 207 had duodenal ulcer. The oldest patient was 67 years of age, and the youngest was 19. The average age was 40.4 years. Thirty of the patients were women and 250 were men. Two hundred thirty-three of these ulcer cases were considered uncomplicated and 47 were complicated, that is, 32 patients had hematemesis and melena and required blood transfusions preoperatively, 7 had symptoms of stenosis with retention and vomiting, and 8 had protected perforation. In 31 cases (14 per cent) of duodenal ulcer partial gastrectomy for exclusion (Finsterer) was done.

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INDICATIONS FOR OPERATIVE TREATMENT

The criteria for the operative treatment of chronic gastroduodenal ulcer were drawn up in cooperation with the medical department where chief internist Römcke and his staff have conducted follow-up examinations of the patients treated medically for many years. After 8 years' observation they found that 22 per cent of patients with gastric ulcer and only 10 per cent of patients with duodenal ulcer had not had recurrence. They have further shown that there is a marked difference in per cent of cure after medical treatment for patients with history of ulcer of under or over 5 years, with much poorer results for those who had symptoms of more than 5 years' duration. Of the latter, only 14 per cent with gastric ulcer and 7.6 per cent with duodenal ulcer did not have recurrence. We therefore recommend operative treatment to all patients having a history of ulcer of more than 5 years' duration. Patients with history of ulcer of less than 5 years are advised to have operative treatment after one course of medical treatment, if they have recurrence, particularly those who do not have the opportunity to follow the recommended diet during their periods of dyspepsia. We do not, of course, recommend operation to patients with lesser complaints which can easily be controlled by dietary means and do not render the patient unfit for work. In cases of gastric ulcer in which the possibility of cancer is present we have become more active than the percentage of cure after medical treatment would seem to warrant.

This increasingly more active surgical view of the treatment of gastroduodenal ulcer has come about not only because of the poor results of the medical treatment, but also in response to the steadily sinking mortality rate after surgical treatment in recent years.

Nicolaysen has shown a decrease in the mortality rate after partial gastrectomy for ulcer from 5.4 per cent in the 10-year period 1933 to 1943 (408 operations) to 0.84 per cent in the 3-year period 1943 to 1945 (236 operations), chiefly as result of better preoperative and postoperative control and treatment. In addition, the good late results after partial gastrectomy for ulcer which are found at follow-up examination must be taken into consideration. Bruusgaard found 90 per cent to be free from symptoms, and Ramberg found satisfactory results in 94 per cent, when the simple anemias of the iron deficiency anemia type which disappear after adequate treatment were excluded.

PREOPERATIVE TREATMENT

Stress is laid upon effecting the best possible physical condition before operation. If there are signs of a very active ulcer, especially if it is large, the patient is given medical treatment until the disease becomes more quiescent. Otherwise we observe the general rules for preparing the patient with blood and fluid control and observation to rule out, recognize, or treat other concomitant diseases before operation.

OPERATIVE TECHNIQUE

Percaine spinal anesthesia according to Seebrecht's method is used because spinal anesthesia with its resulting complete relaxation of the musculature and contraction of the intestines makes operation easier.

The Moynihan II method is used, that is, the anastomosis is placed anterior to the colon with the efferent loop on the lesser curvature, using a comparatively short loop, about 20 to 30 cm. long.

We use clamps and two layers of sutures, continuous catgut and linen in the anastomosis. We do not believe it is important whether clamps are used or not, whether suturing is done in two or three layers, or whether the efferent loop is placed upon the greater or lesser curvature. We use the method described because it is the simplest and easiest. The important point is that the operator must learn one method and use it exclusively; in other words, he must master the method he uses.

In duodenal ulcer we make no attempt to remove the ulcer if it appears to be difficult. If the infiltration and infection surrounding the ulcer are such that we cannot be certain of accomplishing a satisfactory closure of the duodenal stump after the stomach and pylorus have been removed, since the autumn of 1945 we have performed a partial gastrectomy for exclusion according to Finsterer's method. We leave 6 to 8 cm. of the canalis and the pylorus after careful removal of the mucous membrane from this part of the stomach. The mucous membrane is severed from the pylorus by diathermy. The stump is inverted with 2 layers of sutures, catgut and linen, and the suture is covered with the capsule of the pancreas.

Marcussen showed by follow-up examination of patients with partial gastrectomy for exclusion that achlorhydria is achieved with the same frequency by this method as by the usual partial gastrectomy. We always make a "large resection" of the stomach, that is, the line of resection begins on the greater curvature in the relatively sparsely vascularized part between the left gastroepiploic vessels and the vasa brevia and continues on a slightly oblique upward line to the lesser curvature.

POSTOPERATIVE TREATMENT

The patients are given about 1,000 c.c., normal saline solution subcutaneously during operation. In uncomplicated cases 2 to 2½ L. of fluid are administered daily by proctoclysis and intravenously the first 2 to 3 days in the form of 1 L. normal saline solution and the remainder 5 per cent glucose solution. In case of gastric retention an equal normal saline addition is given. We thus attempt to hold the urinary output at about 1 L. Blood transfusions are not given routinely either during or after operation. If there are signs of more than the usual blood loss either during or after operation, blood transfusion is given immediately. The blood loss is estimated and a like quantity of blood is supplied by transfusion. It is important to be aware of the fact that an estimation of the amount of hemorrhage is likely to be

made too low, and one must bear in mind that the postoperative blood loss from the gastrojejunostomy may be considerable.

Routine laboratory tests for hemoglobin per cent and serum proteins are made before operation and on the third postoperative day in uncomplicated cases. Fretheim demonstrated that regularly in the uncomplicated cases of partial gastrectomy there are decreases in hematocrit and serum protein concentrations which reach their lowest level from the second to fourth day after operation, after which they rise to about the preoperative level in the course of 10 to 15 days (Fig. 1).

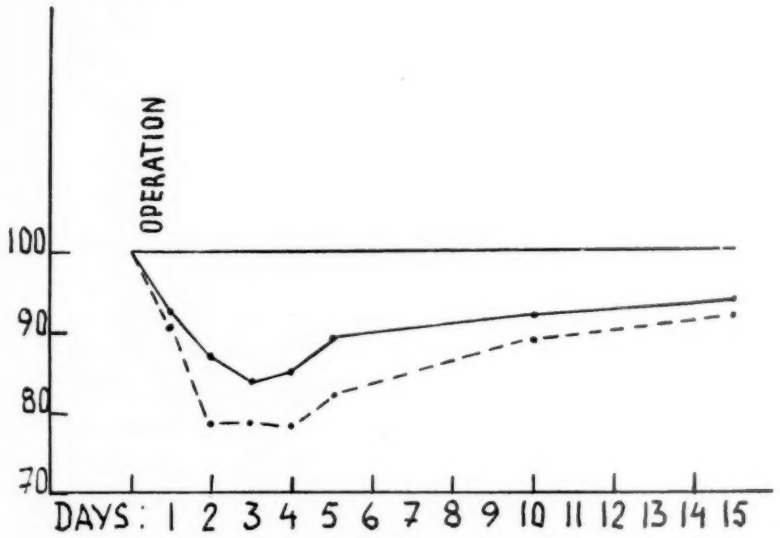

Fig. 1.—Serum protein concentration in gram per cent (———) and hematocrit (– – –) preoperatively and postoperatively after uncomplicated partial gastrectomy for ulcer. The preoperative value is computed on the basis of 100 (Fretheim).

In complicated cases, particularly when the blood loss is greater than usual, the fall in hematocrit and serum protein concentration levels is greater and of longer duration but still approximately parallel, except in certain severe cases with threatened or actual shock in which there is a rise in hematocrit level simultaneous with a fall in serum protein concentration. However, by clinical observation of the patients, with careful attention to signs of hemorrhage, the amount of blood loss may be estimated more quickly than by depending on laboratory findings alone. The hematological changes are first demonstrable after 24 hours or more, by which time the treatment of the hemorrhage should long since have been accomplished. We check for satisfactory treatment by frequent blood examinations.

The oral feedings begin the day after operation in uncomplicated cases with water and carbonated water by teaspoonfuls. Soup is added on the second day, 2 rusks and sweet tea the third day, and 2 fish balls on the fourth day, after which there is a gradual increase to puréed foods.

We do not aspirate the patients routinely, but upon the slightest symptoms of retention aspiration twice a day is instituted and continued until the retention is overcome. An enema is given routinely on the third postoperative day unless the bowels have moved since operation. If flatus is not passed within 48 hours after operation, Prostigmine is given and a rectal tube is inserted at the same time. If the oral intake is insufficient after 5 or 6 days so that fluids must be given parenterally, vitamin B complex and vitamin C are given with the fluids. The patients are urged to move about in bed as soon as possible. As a rule ambulation is not begun before the third day after operation.

POSTOPERATIVE COMPLICATIONS

The postoperative course in the whole study was considered uncomplicated in 197 cases and complicated in 83 cases (30 per cent). The complications included are seen in Table I.

TABLE I

COMPLICATIONS		DEATHS
Hematemesis and/or melena	22	
Intraperitoneal hemorrhage	1	1
Postoperative gastric retention	32	
Diarrhea	6	
Rupture of the incision	13	
Intestinal obstruction	1	
Duodenal fistula	2	
Infection of the incision	5	
Respiratory infection	30	
Thrombosis	8	
Total number of patients with postoperative complications	83 (30%)	1 (0.35%)

Hemorrhage.—Hemorrhage from the gastrojejunostomy which always follows partial gastric resection is not included. Only hemorrhages found clinically to be more severe than usual are included. The usual uncomplicated partial gastrectomy is not followed by postoperative hematemesis. If the stomach is aspirated routinely morning and evening, markedly bloodly stomach contents are found on the first day, after which the blood content decreases without signs of fresh bleeding until the third day when about 100 c.c. greenish gastric content is withdrawn from the fasting stomach upon aspiration in the morning. If there is a large or protracted hemorrhage, one finds in addition to general signs of hemorrhage that the patient feels ill, is nauseated, and regurgitates or vomits bloody stomach contents. This is often accompanied by retention of unusually long duration, or if the blood is passed into the intestine, by melena and frequently diarrhea. In a few cases there has been no unusual bleeding in the early postoperative period, but hematemesis appeared about the tenth postoperative day. This was probably a demarkation hemorrhage from the gastrojejunostomy. The remainder of the hemorrhages occurred during the first and occasionally the second day after operation. There was hemorrhage in only one case on the sixth day as result of heparin treatment for thrombosis.

We have been particularly careful in our clinical observation of our patients as regards increased or repeated hemorrhage and have instructed the nursing staff to report immediately any signs of such complication. We have given blood transfusions as soon as possible in the amounts of the estimated blood loss. At the same time we followed the blood changes with daily laboratory tests. In spite of our care in the matter of hemorrhages, we have found by routine blood tests that in 5 apparently uncomplicated cases the fall in hematocrit and serum proteins was greater than "normal," and these patients were then given blood transfusions. In cases of known hemorrhage we found also that we had a tendency to underestimate the blood loss.

The only death in this series of 280 partial gastrectomies for ulcer was primarily the result of intraperitoneal hemorrhage from the left gastric artery. The patient was a 56-year-old man who developed pneumonia the day after operation. He became afebrile after penicillin treatment in the course of 3 days. He had continuous total gastric retention postoperatively, and in spite of adequate treatment his condition became steadily worse, and death occurred on the seventh postoperative day. Post-mortem examination revealed a huge hematoma on the right side posterior to the anastomosis, where undoubtedly the mechanical conditions as much as the hemorrhage itself caused the lethal outcome.

Postoperative Gastric Retention.—As mentioned before, our patients are not aspirated routinely in the postoperative period, but if signs of retention such as nausea, eructations, or regurgitation appear, we insert a stomach tube and aspirate morning and evening until retention ceases. In this manner one-half of the patients avoid aspiration. Of the other one-half about 20 per cent of the patients were aspirated 1 day, 20 per cent for 2 days, 3 per cent for 3 days, and 3 per cent for 4 days. The remaining 4 per cent of the patients were aspirated longer—24 days in one case. We have included retention as a postoperative complication if more than 100 c.c. was aspirated on the third postoperative day. In a few cases we inserted a duodenal tube into the stomach for a few days. We hesitate to do this because of the danger of complications from the respiratory tract.

Not included in this group is one case of postoperative intestinal obstruction which began 14 days after operation in a 65-year-old patient. This patient had a total rupture of the incision on the first postoperative day and was resutured. A laparotomy was performed on the twenty-fourth day after the partial gastrectomy. The adhesions were released, and the further course was uncomplicated.

Diarrhea.—Diarrhea of more than 3 days' duration occurred in 6 cases. No special cause was found in 3 cases, while in the other 3 cases the possible reason was hemorrhage.

Rupture of the Incision.—In 2 of the cases rupture of the incision was only partial in that the cutaneous layer remained in place. A bloody-serous fluid seeped out, and healing followed with formation of a ventral hernia. In 11 other cases there was complete rupture of the incision with eventration of

the intestines. This occurred within the first 12 postoperative days, most frequently at about the seventh day. All patients were resutured with through-and-through metal suture material in one layer. Primary healing resulted in all cases after the secondary closure, and the further course was uncomplicated except in the one case described previously, in which an adhesion obstruction developed.

When the rupture of the incision occurs within the first 5 postoperative days, it may be considered the result of mechanical causes, but when the rupture occurs later, it must be assumed that the patient's general condition is the chief cause. The most important complications preceding rupture of the incision are shown in Table II.

TABLE II. POSTOPERATIVE COMPLICATIONS PRECEDING POSTOPERATIVE RUPTURE OF THE INCISION

Postoperative hemorrhage	3
Hemorrhage and pneumonia	1
Pneumonia	4
Gastric retention	2
No specific complications	3

An important cause of rupture of the incision is hypoproteinemia. We found in our cases upon examination on the day of the rupture that the hemoglobin per cent was between 75 and 100 and serum protein concentration between 5.1 and 6 Gm. per cent, a markedly reduced level for both, but in many cases of partial gastrectomy with other complications we found values as low or lower, though these patients showed no signs of delayed healing of the incision.

Duodenal Fistula.—Duodenal fistula occurred in 2 cases, both following partial gastrectomy for exclusion with drainage. In both cases there was a marked digestive action upon the skin of the abdomen, but after suction drainage of the fistula was instituted, rapid healing of the skin and improvement of the patient's general condition followed. The fistula remained open for 4 weeks in both cases. The probable reason for the fistula in both cases was a too complete devascularization of the seromuscular cuff, because the decision to perform a partial gastrectomy for exclusion instead of the usual partial gastrectomy was made too late.

Respiratory Infections.—All tracheobronchitis and pneumonia is included, a total of 30 cases. In the first part of the study all patients were treated with penicillin, but in a number of cases the results were uncertain, while good results were obtained with sulfadiazine. It is often difficult to give sulfonamides orally the first few postoperative days, in which cases they were given intravenously twice a day together with intravenous fluids. In the latter part of the study we gave both penicillin and sulfonamides simultaneously for serious postoperative lung complications in order to control the infection as rapidly as possible.

Thrombosis.—Eight cases of thrombosis occurred, and all were treated with heparin as soon as the diagnosis was made. The heparin treatment had to

be discontinued the day after it was begun in one case, because the patient had a large hematemesis. In the other cases the treatment was continued until the patient was afebrile and ambulant. Prophylactic measures were movement in bed and deep breathing as soon as the patient had recovered from the anesthesia. Ambulation was comparatively early, usually the third day if the patient's condition permitted.

DISCUSSION

In a series of 280 partial gastrectomies for ulcer in the 4-year period 1946 to 1949 the course in 197 cases was uncomplicated, while there were complications in 83 cases (30 per cent). One death occurred in the period (0.35 per cent operative mortality rate). Compared with the period before 1943 there was a marked fall in the number of postoperative complications as well as in the mortality rate. However, there were still complications after 30 per cent of the operations, and the chief reason for the better results appears, according to our experience, to be that we now are better aware of the causes of the complications and seek to prevent them and that we are better able to control the postoperative complications. In addition to the general measures with preoperative treatment, postoperative fluid balance and liberal use of blood transfusions, prevention and treatment of infections, early ambulation, and heparin treatment for thrombosis and embolism, there are three other things to which we attribute the markedly improved results in the last few years.

1. On the basis of investigations made we have become aware of the importance of the postoperative hemorrhage from the gastrojejunostomy in relation to the postoperative complications, not only because the hemorrhage itself may be dangerous, but because the secondary results may be the contributing causes of gastric retention, diarrhea, and rupture of the incision. We have steadily become more meticulous with the hemostasis in the anastomosis, but we have often found in spite of this precaution that marked hemorrhage occurred. We believe that it is most important that liberal quantities of blood be administered at once without awaiting results of laboratory blood tests, which are misleading at first, since the greatest changes are first seen 2 days after the hemorrhage.

2. Peritonitis resulting from leakage of the duodenal stump was earlier a fairly frequent cause of death. Since the autumn of 1945, when we began to perform partial gastrectomy for exclusion according to Finsterer's method in cases of difficult duodenal ulcers, we have had no deaths from this cause. In the 10-year period from 1933 to 1943 a total of 11 of the 22 postoperative deaths were caused by peritonitis, 7 as result of leakage from the duodenal stump.

3. The improved results seen here in recent years are not due to improved technique, since the operations are performed by both the chief of staff and his changing residents. We are prone to consider the improvement a result of the teamwork which has been established in the department, in which both

the surgeons and the nurses have become "stomach-minded." One of Visick's "house surgeons" expressed the same opinion as follows: "Provided that the chief is in moderately good operating form, I can keep his patients alive so long as sister is not away for the week-end." We agree with the late Mr. Visick.

SUMMARY

A series of 280 partial gastrectomies for ulcer was analyzed, with special emphasis upon the causes and treatment of the postoperative complications. The mortality rate was 0.35 per cent, and the postoperative complications occurred in 30 per cent of the patients. The most important complications were postoperative hemorrhage, gastric retention, rupture of the incision, and respiratory infections. It is shown that the marked improvement in the results in recent years is due not only to a more effective treatment of infections (sulfonamides and penicillin), but probably primarily to the general measures used in preoperative and postoperative treatment in which special stress is laid upon the frequently large hemorrhages from the gastrojejunostomy and treatment by ample blood transfusions. In the second place, the improvement is the result of the change to partial gastrectomy for exclusion by Finsterer's method in cases of duodenal ulcer difficult to remove. The fact that both the surgeons and the nurses are "stomach-minded" is also of great importance.

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DIVERTICULITIS OF THE COLON AND ITS SURGICAL MANAGEMENT

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IN SPITE of the existence of an extensive literature on the subject of diverticulitis of the colon, there remains considerable misunderstanding regarding the proper management of its surgical complications. The surgeon meets the condition all too frequently; on occasion he is faced with grave decision as to proper procedure. I can think of no abdominal conditions which call for more individualization or for keener surgical judgment than do the complications of diverticulitis. The relatively high incidence of serious complications was appreciated only after an extensive review of literature on the subject. A comprehensive analysis of various methods of treatment and prognosis has been undertaken to assist further in securing satisfactory answers to the remaining unsolved problems.

Diverticulosis was described nearly a century ago by Virchow;[1] the disease, nevertheless, is comparatively new to the surgeon. Virchow recognized and described diverticulitis as a disease entity in 1853. He is credited with having described certain inflammatory areas of the colon, which he called "isolated circumscribed adhesive peritonitis." Diverticulitis of the colon was considered a rarity. Prior to the turn of the century, the condition was looked upon as a rare pathologic curiosity with only isolated cases reported.[2, 3] Surgical interest in diverticulitis of the colon was not aroused in this country until 1907 when Mayo[4] first reported to the meeting of the American Surgical Association the resection of the sigmoid colon in five cases of chronic obstructive diverticulitis at the Mayo Clinic.

It was not until the general use of barium x-ray studies of the colon that a diagnosis of diverticulitis could be established preoperatively. In 1915, Case[5] demonstrated diverticula of the colon with roentgen-ray studies following a barium meal. At the same time Carman,[6] working independently, demonstrated multiple diverticula of the colon by roentgenographic studies following barium enema. With the improved roentgen-ray technique and the wider use of the barium enema, it was found that diverticulosis of the colon was much more common than was formerly supposed to be the case. In 1925, Spriggs and Marxer[7] found diverticulosis of the colon in 100 out of 1,000 consecutive radiographic examinations. In 1927, they made another important contribution to the literature on the subject.[8] Utilizing the barium enema with roentgenologic studies, they described the characteristics of the prediverticular state as spastic with a ragged outline. They described the characteristic "spiked" or "saw-toothed" appearance of the diseased colon. Their description is still quoted by the authors of today. Since their work, roentgen-ray study has become the only reliable method of diagnosing colon diverticula.

This study is an abridgment of a thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania toward the requirements for the degree of Master of Medical Science for graduate work in surgery.

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ETIOLOGY

The etiology of diverticulitis of the colon is unknown. Several explanations have been offered, the more common of which are as follows: old age,[9] obesity,[9] constipation,[1] congenital or hereditary defects,[11-15] sympathetic nerve imbalance to the colon,[16] inherent weakness of the colon, and increased intracolonic pressure.[2, 17-20] Extensive anatomic studies and experimental work have been carried out on the colon to find the cause. No single factor was enough to explain the origin of diverticula. The most widely accepted theories assume a combination of the fundamental factors of weakness of the colon wall and of increased pressure from within. This increased colonic pressure is the causative factor which provokes herniation of the mucosa through points of least resistance of the defective colon wall. Dixon[21] stated that such herniation is produced by contraction occurring simultaneously both distal and proximal to a normal bowel segment. The cause of the weak points is unknown. Some assume that the inherent weakness of the colon musculature has existed since birth and is congenital in origin.[12, 13, 14] Others claim that heredity should be included as a major causative factor in the etiology. Since the disease is rarely seen before the age of 40, the most plausible explanation of the weakness is loss of muscular tone which is characteristic of the degenerative period of life.[22] The weak points are found where the nutrient blood vessels pass through the muscular wall.[17, 23] In support of this, diverticula of the colon are usually found along the mesenteric border. It is probably safe to assume that the muscular weakness, whether congenital or acquired, is the fundamental factor, and increased intracolonic pressure is perhaps the exciting cause in the production of diverticula. This is further substantiated by the fact that the sigmoid and descending colons are the most common sites of diverticula, while the remainder of the colon and rectum is rarely involved in the disease.[16, 17, 20, 24-26] The highest colonic pressure is exerted in the sigmoid colon because of its thicker muscular walls, greater activity, smaller diameter, and the solid character of the fecal stream at this level. After careful consideration of all the explanations, the most likely conclusion seems to be that the outstanding features of the formation of colon diverticula have to do with inherent weakness of the muscular walls plus increased intracolonic pressure which results from constitutional or environmental causes.[19]

PATHOLOGY

Diverticula of the colon are of the acquired or false variety whose walls consist of mucosa, submucosa, and serosa. The diverticulum mucosal sac herniates through the muscularis, near the mesenteric border, along with, or closely associated with, the lymphatics and blood vessels.[21, 23] It has been stated that once the process is started it cannot be arrested, but that the diverticula increase in size and number.[23] The size ranges between 1 mm. and 2 cm. in diameter, and in the presence of infection may be much larger.[28] The condition in which uninflamed sacs occur is spoken of as diverticulosis, but when the sacs are involved in an inflammatory process it is called diverticulitis.

The diverticula are round in shape when small, but as they grow larger they assume an oval, flask shape, with a definite neck at their attachment to the bowel.[18] When the uninflamed diverticulum contains fecal material within the sac, it has a typical dark bluish appearance.[29] The small neck opening into the lumen of the bowel may act as a mechanical barrier to the expulsion of the fecal contents which enter the sac, especially since there is no muscle in the wall of the sac to aid in expelling its contents. The liquid or semiliquid feces which enter the sac may become inspissated, forming a fecalith which damages the mucosal lining of the sac wall, thus providing a portal of entry for infection. The ensuing edema may impair the blood supply, causing gangrene of the sac wall, as is sometimes seen in an inflamed appendix or gall bladder. In the presence of infection, the nonsymptomatic diverticulosis becomes a diverticulitis. The inflammatory process may extend to the surrounding bowel wall, the muscularis, or to adjacent organs. Such an inflammatory process in the sigmoid colon may give symptoms described as "left-sided appendicitis."[30]

Histologically, an uninflamed diverticulum reveals a normal mucosa and serosa. In the presence of infection, which may be limited to the diverticulum, it becomes enlarged with leucocytic infiltration of its walls and atrophic changes of the mucosa with thickened opacity of the serosa. The gross changes show extension of the inflammatory process along the colon wall. These changes are characterized by marked fibrous infiltration of the submucosa and muscularis. These fibrotic inflammatory changes in the outer coats of the bowel may result in a narrowing of the lumen with partial or complete obstruction, while the mucosa remains relatively normal. The involved segment of colon is usually much greater than that produced by carcinoma, which causes the obstruction from a small annular growth within the lumen of the bowel, while the outer coats remain relatively uninvolved.

INCIDENCE

The incidence of diverticulosis of the colon in persons over 40 years of age is probably more frequent than is generally recognized because uncomplicated diverticulosis rarely gives symptoms. W. J. Mayo[16] in 1930, at the Mayo Clinic, reported that 5 per cent of post-mortem examinations of persons over 40 years of age showed diverticula of the descending colon and sigmoid. At the same time Rankin and Brown[24] reported the same percentage on patients over 40 years of age studied roentgenographically. It was noted that the sigmoid colon was involved in 75 per cent of the cases. According to Sauer,[9] in statistics compiled from the literature, diverticulosis was found in 5.2 per cent of 70,572 colons examined at necropsy or roentgenographically. Ochsner and Bargen[31] in 1935 made x-ray studies of 2,747 patients at the Mayo Clinic and reported that 7 per cent showed diverticula.

Most authorities agree that diverticulitis is rare before the age of 40. Bailey[32] stated that about 95 per cent of patients with the disease are past 40 years of age. The over-all average age of patients with diverticulitis is about

55 years.[28] Opinion as to sex predominance varies. Most authorities indicate that diverticulitis is equally distributed between sexes. However, some report that the disease occurs more frequently in the male. It is estimated that 5 per cent of patients over 40 years of age have diverticulosis, and that 15 or 20 per cent of these will develop diverticulitis.[18, 20, 24, 31, 34] It is the consensus of opinion that about 20 per cent of patients with diverticulitis will develop complications requiring surgery.[17, 35, 36]

SYMPTOMATOLOGY

The symptoms of diverticulitis of the colon are variable, depending on the location of the disease and the degree and extent of the inflammatory process. Mild inflammatory lesions may cause no symptoms, but, as the inflammation spreads along the bowel wall, there may be mild abdominal soreness or slight low abdominal cramps, flatulence, constipation, diarrhea, or, occasionally, rectal bleeding, depending on the stage of the disease. The classical symptoms of acute diverticulitis of the sigmoid colon are easily recognized. They are not unlike those of acute appendicitis except that the symptoms are referable to the left lower quadrant of the abdomen. The condition is sometimes referred to as "left-sided appendicitis." If one encountered the textbook picture of pain in the left lower quadrant of the abdomen, nausea, vomiting, flatulence, slight distention, tenderness, muscle guarding or slight rigidity, a palpable mass in the left lower quadrant, leucocytosis, and a low-grade fever, the diagnosis would be simple. Unfortunately, this classical chain of symptoms is not always present, and may vary greatly with individuals or within the same individual, depending on the location, the extent, and severity of the attack. Even when there is increasing severity of all symptoms, the pain becoming colicky and the palpable mass presenting in the left lower quadrant, if appropriate medical treatment is instituted the symptoms may subside with a disappearance of the signs of acute inflammation and a gradual decrease in the size of the mass. In connection with the symptomatology of diverticulitis, I should like to quote Young and Young[35] in the following passage:

"As the disease progresses, the symptomatology becomes more marked. There is distinct abdominal pain, usually in the lower half of the abdomen being not infrequently localized in the left lower quadrant and sometimes in the right lower quadrant. There is history of irregular bowel habits, constipation and diarrhea, occasionally bleeding and, rarely, small stools. There may be a feeling of incomplete or unsatisfactory bowel movements on the one hand, or relief of symptoms following defecation on the other hand. Nausea and vomiting are not infrequent. Some patients have frequency, nocturia or burning, giving rise to a suspicion of disease of the urinary tract. There is frequently tenderness on palpation, usually in the lower abdomen. Fever and leukocytosis are more frequent in the severe cases than in the mild ones."

In severe cases of diverticulitis without subsidence of the inflammatory process, a sudden sharp acute pain in the abdomen suggests rupture of a diverticulum into the free peritoneal cavity and generalized peritonitis with shock, rapid thready pulse, rigidity, and fever, a situation which carries a

high mortality. On the other hand, when adhesions have formed previously, which is the rule, a localized intra-abdominal abscess may follow the perforation or slow leak. This abscess may resolve, dissect through the abdominal wall, producing an external fistula, or perforate into an adjacent organ. The sudden disappearance of the tender mass, relief of pain, and the appearance of flatus and pus from the urethra indicates rupture into the bladder with the formation of a sigmoidovesical fistula. The sudden disappearance of the mass and the passage of pus from the rectum suggests perforation into the distal colon or rectum.

The most frequent signs and symptoms encountered are those seen in chronic diverticulitis which develop slowly over several days or weeks. Intermittent colicky pain, constipation, and abdominal distention may gradually become worse and lead to partial or complete large bowel obstruction with all the accompanying signs and symptoms so ably described by Wangensteen.[37] The abdomen may be moderately or markedly distended, depending upon the location, degree, and duration of the obstruction. Roentgenographic studies should locate the level of the obstruction and show the degree of distention. The palpation of a tender, hard mass coursing in the direction of the sigmoid colon is strongly suggestive of diverticulitis.

A word should be said about hemorrhage since it constitutes an interesting manifestation of diverticulitis. The fact that rectal bleeding is seen in both carcinoma and diverticulitis of the colon makes it important in the differential diagnosis. The passage of gross blood in colon diverticulitis is not a rarity as early writers would have had one believe.[7] Statistics report gross rectal bleeding to occur in between 5 and 22 per cent of cases. Most authorities now agree that bleeding occurs in diverticulitis about as frequently as it does in colon carcinoma.

Although cecal diverticulitis is rare, it should always be considered when dealing with abdominal right lower quadrant pain. In 1940, Jonas,[41] at Johns Hopkins Hospital, reported solitary diverticulitis of the cecum in three cases. He reviewed the literature and found 15 cases reported up to that time. Costin and Gaston,[42] in the most recent review of the literature, found 99 cases and reported 2 new cases, making a total of 101. I am reporting one case in this communication, bringing the total to 102. The general surgeon probably sees more patients with abdominal right lower quadrant pain than any other condition and probably operates for right lower quadrant pathology more often than in any other region. Diverticulitis of the cecum more closely resembles appendicitis than any other entity, and yet the disease is seldom considered in the differential diagnosis. The diagnosis of cecal diverticulitis is rarely made preoperatively and, should one make this diagnosis, it should be confirmed at the operating table. It should be borne in mind that a redundant sigmoid colon may occupy the right iliac fossa and, should it become involved in an inflammatory process while in this location, the symptoms may be identical with those seen in appendicitis. If the differential diagnosis cannot be made, exploration is indicated.

DIAGNOSIS

All agree that the diagnosis of diverticulitis depends upon the roentgen demonstration of the diverticula and that in the absence of x-ray findings the diagnosis is not justified. There are many abdominal conditions that must be considered in the differential diagnosis. Bockus[28] includes carcinoma, hyperplastic tuberculosis of the colon, acute appendicitis, ulcerative colitis, ileocolitis, pelvic inflammatory disease, actinomycosis, syphilis, and perinephritic abscess. To this one may add amebiasis, acute cholecystitis, duodenal ulcer, ureteral stone, cystitis, twisted ovarian cyst, uterine fibroid, and tubal pregnancy. It is extremely difficult to differentiate perforated diverticulitis from perforated appendix, perforated peptic ulcer, and ruptured ectopic pregnancy. Usually a mistaken diagnosis of ruptured appendix is made and the true pathology discovered at operation.

I shall not discuss all the conditions to be ruled out in the differential diagnosis, but will limit this paper to the most common conditions encountered.

Carcinoma.—Chronic diverticulitis is most often confused with carcinoma of the sigmoid colon. The patients are in the same age group. Both have lesions most frequently involving the left side of the colon; both may have gross rectal bleeding, and in both cases the disease may produce tumors of the sigmoid with obstruction. It is said that from 1.7 to 8 per cent of colon carcinomas have an associated diverticulitis.[18] Carcinoma of the colon runs a drawn-out, downhill course without remissions, while patients with diverticulitis are usually in good condition and the course is intermittent, with recurrent flare-ups. Diverticulitis is more likely to occur at a higher level, the sigmoid colon being involved in 80 per cent of the cases, while the rectum is seldom, if ever, involved. On the other hand, carcinoma most frequently involves the rectum and rectosigmoid colon. In carcinoma, the involved segment of colon is short; the tumor arises from the mucosa, forming an annular, painless lesion that is freely movable. Diverticulitis usually causes a painful inflammatory tumor involving the outer coats of a relatively long segment of colon, which is likely to be tender, with limited mobility. There is usually an elevated temperature and a leucocytosis. The roentgenologist is most helpful in clarifying the diagnosis by means of the barium enema. In carcinoma of the colon, the lesion is most often confined to a short segment of bowel, with a clear-cut, narrow filling defect, and a typical napkin ring deformity. On the other hand, in diverticulitis, there is usually a much longer segment of the colon involved, with saw-toothed serrations and a narrowing lumen with normal mucosa presenting its typical feathery appearance. Counseller[17] stated that sigmoidoscopy is frequently an aid in arriving at the correct diagnosis. He listed the five following signs as indications of diverticulitis: "1. Limited mobility of a segment of the bowel that normally is freely movable; 2. angulation of the upper part of the rectum because of inflammation; 3. reduced lumen and adherent mucosal folds; 4. sacculation of the sigmoid; and 5. rectal visualization of the diverticula."

Acute Appendicitis.—Diverticulitis of the cecum, or of a redundant sigmoid located and adherent to the right iliac fossa, may simulate acute appendicitis. Even with a history of previous attacks of diverticulitis that have

been diagnosed roentgenographically, it is often impossible to differentiate them preoperatively. One must bear in mind the possibility of concomitant acute appendicitis with diverticulitis. The differential diagnosis is seldom made preoperatively, and, when doubt exists, exploration is indicated.

Pelvic Inflammatory Disease.—Acute salpingitis can mimic diverticulitis and often the surgeon is hard-pressed to differentiate the two conditions. A left pyosalpinx may give a tender palpable mass in the region of the sigmoid and quite often it becomes attached to the sigmoid. In a similar manner, acute diverticulitis of the sigmoid may become attached to the uterus and adnexa. One should remember that salpingitis is rarely encountered after the age of 40 and that diverticulitis is seldom seen before the age of 40. As a rule, one does not encounter bowel symptoms, such as partial or complete obstruction, in adnexal disease, yet it is not uncommon in diverticulitis. The burning on urination and vaginal discharge, so characteristic of salpingitis, is not usually a feature of diverticulitis. A rectovaginal examination should always be included as part of the pelvic examination. Quite often the examiner, by means of the rectal finger, may move the inflamed colon separate from the adnexa. On the other hand, if there is a tubo-ovarian mass, it may be moved independently of the bowel. Here, too, the x-ray studies following barium enema can be most useful. The typical saw-toothed serrations in colonic diverticulitis are conclusive.

Ulcerative Colitis.—In ulcerative colitis the differential diagnosis should be no problem if the characteristic x-ray findings are kept in mind. Here, with the aid of the sigmoidoscope, the diagnosis should be clinched by direct vision of the typical lesions of ulcerative colitis.

SURGICAL MANAGEMENT

It is estimated that approximately 85 per cent of the patients with diverticula should have medical management. This paper will deal with the remaining 15 per cent who will require surgical management. Most authorities agree that surgery should be reserved for the complications of diverticulitis. They list six general indications for surgery as follows: (1) acute perforation, (2) abscess, (3) obstruction, (4) fistula formation, (5) coexisting carcinoma, and, finally, (6) inability to differentiate diverticulitis and carcinoma. To this should be added cases in which the diagnosis cannot be definitely established, and where the possibility of some other condition requiring an emergency operation exists, that is, acute appendicitis, perforated peptic ulcer, ruptured ectopic pregnancy, twisted ovarian cyst, and volvulus of the sigmoid colon. There is general agreement as to the indications for surgery listed above, but there is still some controversy as to the proper surgical procedure to follow for the various complications encountered. It is surprising that the actual surgical management has changed very little since 1907, when Mayo first reported, in this country, the successful resection of the sigmoid colon for diverticulitis. The following quotation, taken from Mayo's[4] report to the meeting of the American Surgical Association in 1907, will give an idea of the early surgical trend: "The surgical treatment of diverticulitis of the colon depends upon the condition present. First, localized suppurative cases

must be treated by force drainage. If, in conjunction with the infective process, acute obstruction of the bowel develops, a temporary artificial anus should be made and, if necessary, after the infection has subsided, the involved colon may be resected. Second, if a considerable tumor is present and the symptoms do not show a tendency to disappear, it is better to make a primary resection of the affected part of bowel, before abscess and fistula supervene to render prolonged invalids." Considering the fact that it has been almost one-half century since this report was given, the progress in the surgical management of diverticulitis of the colon has not been remarkable. When one notes the great strides that have been made in other abdominal conditions of a surgical nature, it becomes evident that the surgical management of diverticulitis has not been ideal. Of course, great progress has been made in all surgery, with improved anesthesia and surgical technique. With a better understanding of body fluid and electrolyte balance, and the introduction of antibiotics, the mortality has been greatly reduced. The surgical management of colonic diverticulitis calls for good judgment and patience on the part of the surgeon and patient.

Acute Perforation.—Perforation into the free peritoneal cavity is the rarest and most serious of all complications of diverticulitis. It is considered an emergency which calls for an immediate exploration. The diagnosis is often difficult and is usually not made preoperatively. The important thing is to recognize it as an acute abdomen and to institute immediate and appropriate treatment, utilizing the simplest surgical procedure, namely, incision and drainage. No attempt should be made to close the perforation, for in most cases the sutures will not hold in the inflamed and edematous bowel wall. Johns[43] advocated closure of the perforation, while Rankin and Grimes[44] recommended performance of a colostomy proximal to the perforation. Others have advised exteriorization of the perforated segment of colon. According to Jones,[45, 46] the surgeon's responsibility in this grave condition is to "save the life of the patient," and simple drainage is his procedure of choice. Supportive measures, such as Wangensteen suction, antibiotics, blood, fluid, and electrolyte replacements, should be instituted.

Localized Abscess.—The most frequent complication of diverticulitis is the so called "chronic perforation," or a slow leak, forming a localized walled-off peridiverticular abscess, which is usually located in the left lower quadrant of the abdomen. Some authorities advocate nonsurgical management with antibiotics, hoping the abscess will disappear spontaneously. However, most surgeons recommend incision and drainage if after a period of about one week the abscess has not decreased in size; and if there is associated pain and fever, such drainage should be carried out by means of the extraperitoneal approach. Care should be taken not to break down the barrier wall and allow the infection to spread. If operation is delayed, at times the abscess may drain into the rectum and heal spontaneously. It may perforate into the bladder, forming a fistula, or break through the abdominal wall or perineal floor forming a fecal fistula. Quite often, following incision and drainage of an abdominal abscess, a fecal fistula results, which necessitates excision at a later date.

Obstruction.—The management of obstruction in diverticulitis depends upon several factors, namely: the general condition of the patient, the degree, location, duration of the obstruction, and the degree of distention. Smithwick[20] stated that all cases of obstruction due to diverticulitis are located in the sigmoid colon. It is generally agreed that most cases of partial and many cases of complete obstruction will subside under conservative treatment consisting of bed rest, withholding fluids by mouth, parenteral fluids, and intubation with Wangensteen suction. When medical management fails to relieve the obstruction, surgical intervention with colostomy is indicated. If the distention is great, there should be no delay in performing a colostomy, because of the danger of perforation of the cecum. The fluid and electrolyte balance should be restored, but this should require little time. If the condition of the patient warrants it, a colostomy can be carried out under local anesthesia. Preliminary cecostomy has been advocated by some as the safest and simplest procedure in these emergencies. The few cecostomies that I have had experience with have been very unsatisfactory. In the first place, the fecal current is not diverted and there is not the rapid disappearance of the inflammatory process, as is seen when the fecal stream is completely diverted by a colostomy in the transverse colon. In the second place, it is impossible to prepare the proximal colon for subsequent surgery with a cecostomy. Lastly, it is not simple to perform a cecostomy in a distended cecum without soiling. On the other hand, it is comparatively simple to perform a loop colostomy in the transverse colon proximal to the obstruction. If necessary, the procedure may be carried out under local anesthesia without discomfort. If the need for relief of the obstruction is urgent, the distention may be relieved almost immediately after the loop is exteriorized by the use of a large needle.

After 24 to 48 hours it is safe to open wide the exteriorized loop. In preparation for subsequent surgery it is a simple matter to irrigate the distal loop effectively. After a period of six months, the distal colon may be studied by sigmoidoscopy and roentgen-ray examination, the results of which should determine the future course. No hard and fast rule can be applied here. I believe the question of further operative procedure will depend on the individual case. The unanimous opinion is that there should be a waiting period of from three months to a year, and that no attempt at resection should be undertaken in the presence of active inflammation. Most authorities give the optimum waiting period as one year.[24, 45, 47] If, after one year, there is no evidence of infection and no narrowing of the lumen, it is safe to close the colostomy in a limited number of cases. On the other hand, if there is x-ray evidence of narrowing of the lumen and the segment of involvement is under 15 or 20 cm., it is advisable to resect the segment with an end-to-end anastomosis, closing the colostomy after about six weeks. If there is a relatively long segment of involved colon, resection may not be feasible, and, in such a case, it may be wise to leave the colostomy. If the patient insists upon closure of the colostomy, he should be informed that, even after resection of the involved segment, there is no assurance that development of diverticula at another segment of colon will not occur. If carcinoma cannot be ruled out, resection is essential if the case is operable.

Fistula Formation.—The various fistulas encountered as complications of diverticulitis constitute an interesting surgical problem, each case calling for individualization on the part of the surgeon. Probably the most frequent fecal fistulas are those located on the anterior abdominal wall in the lower left quadrant. These cutaneous fistulas are the residue of diverticular abscesses which have been drained surgically or have opened spontaneously. Under conservative management, many of these fistulas will close spontaneously after six months to a year. At times it is necessary to investigate the fistulous tract by injection of Lipiodol, followed by x-ray studies. A few of these tracts may be dissected out and the opening in the bowel closed. However, most observers are of the opinion that a colostomy should be performed in the transverse colon, proximal to the fistula, if it has not closed after a six months' waiting period. After the fecal current has been diverted and the distal loop prepared, the tract and involved segment of colon should be resected with an end-to-end anastomosis. It is then safe to close the colostomy after an additional six weeks. Fortunately, perineal fistula is a rare complication of diverticulitis, but when present it constitutes a more difficult surgical problem, which in general should be handled in a similar fashion, as outlined above. Rectocolic fistulas do not require surgery, as they all heal spontaneously. A sigmoidovesical fistula is not a rare complication of diverticulitis. Once it develops, an immediate colostomy in the transverse colon should be performed to sidetrack the fecal stream, which will usually result in a spontaneous closure of the fistula. After a waiting period of one year, x-ray studies, sigmoidoscopic and cystoscopic examinations are done to evaluate the condition of the sigmoid and bladder, and if there is no narrowing of the lumen and no evidence of infection, it may be feasible to close the colostomy. On the other hand, if there is residual infection or narrowing of the sigmoid lumen, resection of the involved segment with end-to-end anastomosis is indicated. The colostomy may be closed six weeks following the resection.

Inability to Differentiate Malignancy.—It is surprising how often the surgeon is confronted with differentiation between diverticulitis and carcinoma. Even at the operating table, with the abdomen open and the lesion visualized, it is sometimes impossible to differentiate the two conditions. This is true especially with cecal involvement. If doubt exists, it is the surgeon's duty to perform a radical resection of the segment of bowel in question.

REPORT OF CASES

CASE 1 (92469).—M. B., a 52-year-old married white woman, was admitted to the hospital July 7, 1949, complaining of abdominal pain, more marked in the right lower quadrant. For the past six weeks she had been having intermittent attacks of abdominal cramps and on several occasions had passed mucus and blood. One week prior to admission the pain became more severe with associated nausea but no vomiting. She had considerable abdominal distention and experienced relief on expelling gas. She had difficulty in getting the bowels to move.

Physical examination revealed a well-developed, slightly obese woman with blood pressure of 140/70, temperature of 101° F., pulse of 90, respirations 20. The abdomen was moderately distended and there was a tender palpable mass the size of an orange in the right lower quadrant. Vaginal and rectal examinations revealed a normal-sized uterus fixed to a tender, firm mass in the right iliac fossa. Red blood count was 3,600,000, hemoglobin 11 Gm., white blood cell count 14,000, stabs 2, segmentals 87, lymphocytes 10. Urine tests showed albu-

min 2 plus, sugar negative, blood chemistry normal. Roentgenographic studies of the colon following barium enema showed numerous diverticula in the sigmoid and distal descending colon. The cecum was never completely filled out due to extreme pain and tenderness. The findings suggested an abscess surrounding the cecum but of course a tumor was not ruled out.

On conservative management with transfusion, chemotherapy, and antibiotics, the temperature returned to normal and there was a gradual decrease in the size of the mass. After three weeks' hospitalization she was discharged much improved with a small nontender mass still palpable on abdominal examination. She did not return in three months for x-ray studies as advised.

Comment.—In the majority of cases, an inflammatory mass will completely subside on proper medical regimen. However, it is sometimes necessary to drain an abscess secondary to a perforated diverticulitis and this may often be followed by a fecal fistula.

CASE 2 (74628).—J. R., a 43-year-old married white woman, was admitted to the hospital Feb. 4, 1948, complaining of abdominal cramps and distention. For the past ten days she had been having cramps, distention, and constipation which had been growing progressively worse. She had not had a bowel movement for the past five days, but on two occasions had expelled gas with some relief. An enema caused extreme pain with no results. On the day prior to admission there had been nausea and vomiting.

Physical examination revealed a well-developed and well-nourished middle-aged woman in acute distress. The abdomen was distended and tympanitic. There were no palpable masses, but tenderness with muscle resistance was elicited in the left lower quadrant. Vaginal and rectal examinations revealed a normal-sized uterus fixed to an indurated, hard, tender mass the size of an orange in the left iliac fossa. The urine was normal, blood chemistry was normal, and the white blood count was 11,200. A scout film of the abdomen showed distention of the colon except the lower sigmoid colon and rectum. Barium enema showed complete obstruction at the upper sigmoid colon.

Exploration through a suprapubic midline incision revealed an inflammatory diverticular mass in the sigmoid flexure adherent to the posterior surface of the uterus. A loop colostomy was made in the descending colon proximal to the involved sigmoid. The colostomy was opened in thirty-six hours and she was discharged after ten days. One year later she was readmitted to the hospital for closure of the colostomy. Proctoscopic examinations and roentgenograms of the distal loop showed no evidence of inflammatory reaction or narrowing of the lumen so the colostomy was closed. Convalescence was uneventful. She was given instructions about diet and bowel habits and discharged on the fourteenth postoperative day. She has remained asymptomatic.

Comment.—A diagnosis of diverticulitis was not made preoperatively. The colostomy should have been made in the transverse colon to facilitate subsequent resection of the sigmoid had it been deemed necessary.

CASE 3 (75691).—E. H., a 59-year-old white man, was admitted to the hospital March 7, 1948, for closure of colostomy. His trouble dated back to 1940, when he began to have attacks of lower abdominal cramps, distention, and a fever with alternating attacks of diarrhea and constipation. At that time a diagnosis of colonic diverticulitis was made. Under a medical regime of diet and regulation of bowel habits, his condition improved until August, 1944, when he was admitted to the hospital complaining of passing gas and fecal matter through the urethra; this was accompanied by burning pain and marked urinary frequency. On this admission the surgeon closed the fistulous communication between the sigmoid and bladder and tacked the thick omentum between these structures. A suprapubic cystotomy was performed at the same time. A short while after being discharged there was a recurrence of the sigmoidovesical fistula. On Sept. 22, 1945, he was readmitted to the hospital and the

fecal stream was diverted by performing a loop colostomy in the transverse colon. Following this procedure the fistula closed spontaneously within a few weeks and he has remained asymptomatic since that time.

On this admission, March 7, 1948, physical examination revealed a well-developed and well-nourished 59-year-old man not acutely ill. Blood pressure was 155/100, temperature 98° F., pulse 74, respiration 18. The abdomen was flat with a well-functioning loop colostomy a little above and to the left of the umbilicus. There was an incisional hernia below the colostomy. The suprapubic incisional scar was well healed. Urinalysis, blood count, and blood chemistry were normal. Cystoscopic examination showed no infection or evidence of fistula. Sigmoidoscopic examination was normal. X-ray studies of the distal loop revealed a movable sigmoid flexure with no signs of inflammation and no narrowing of the lumen.

The colostomy was closed under spinal anesthesia and the incisional hernia repaired. The postoperative convalescence was uneventful and he was discharged on the twelfth postoperative day with instructions about diet and bowel habits. He was warned about the possibility of a recurrence. About eight months following the closure of the colostomy, while on a hunting trip eating highly seasoned foods and consuming alcoholic beverages, he had a recurrent mild attack of lower abdominal pain. This attack was controlled with a few injections of penicillin and for the past two years he has remained asymptomatic.

Comment.—It is unwise to attempt to close a sigmoidovesical fistula in the presence of inflammation. If the fecal current is diverted by a colostomy proximal to the fistula, preferably in the transverse colon, most fistulas will close spontaneously. In this case it probably would have been wiser to have resected the involved sigmoid colon with an end-to-end anastomosis before closing the colostomy, particularly so since the advent of streptomycin and aureomycin, which almost completely remove the infective hazard from open resections of the large bowel.

Case 4 (81125).—L. P., a 69-year-old white man, was admitted to the hospital Aug. 8, 1948, at 3 A.M., in shock from a massive bowel hemorrhage. He had been in good health until two weeks previously, when he first began to complain of abdominal cramps. One week prior to admission he passed a tarry stool. At 1:30 A.M. the morning of admission, he was awakened with abdominal cramps and a desire to defecate, and, on going to the bathroom, he passed a large bloody stool and became weak and dizzy. An ambulance was summoned and, on arriving at the hospital, he passed another bloody stool. On admission the skin was clammy, blood pressure 80/40, pulse 140, red blood count 3,000,000, hemoglobin 9 Gm. The abdomen was flat with slight resistance over the lower part. There were no palpable masses. Rectal examination was negative except for blood on the examining finger. He was immediately transfused with 500 c.c. of blood and came out of shock. The following day he was given another 500 c.c. of blood. There was no more bleeding after admission. Forty-eight hours later x-ray studies following a barium enema showed extensive diverticulitis of the entire colon. X-ray studies of the upper gastrointestinal tract were negative. He was placed on a medical regimen and discharged after eight days' hospitalization. There have been no episodes of hemorrhage or other gastrointestinal complaints since that time.

Comment.—Massive hemorrhage can be a serious complication of colonic diverticulitis. At this age it is extremely important to rule out carcinoma, since hemorrhage is common in the latter disease.

Case 5 (81007).—H. W., a 46-year-old white man, was admitted to the hospital Aug. 5, 1948, complaining of pain in the right lower quadrant of the abdomen with nausea and vomiting. About 48 hours before admission he had noticed the gradual onset of continuous pain over the lower abdomen which later localized in the right iliac fossa. Bowel movements had been regular with a normal one a few hours before admission. He was known to have

diverticulitis, having been admitted to the hospital three times in the past eighteen months for treatment of this disease. The diagnosis had been confirmed by roentgenogram. All previous attacks were characterized by colicky pain in the left lower quadrant accompanied by gas and abdominal distention.

Physical examination revealed a middle-aged man acutely ill. The abdomen was flat, with marked tenderness and muscle spasm in the right lower quadrant and with the maximum findings at McBurney's point. There were no palpable masses. Rectal examination revealed tenderness high on the right. Temperature was 101° F., white blood count 20,000, stabs 1, segmentals 74, lymphocytes 17, monocytes 2. Even with the known previous attacks of diverticulitis, acute appendicitis could not be ruled out, so an immediate exploration was performed through a low right rectus muscle-splitting incision. On opening the abdomen numerous diverticula were demonstrated through the colon, especially in the sigmoid. There was a firm inflammatory diverticular mass 5 cm. in diameter located on the anterior cecal wall just distal to the ileocecal valve. The omentum was adherent to this mass. The appendix and adjacent cecal wall were not involved so it was felt the appendix could be safely removed with little danger of a fistula resulting. The appendix was removed and the postoperative course was uneventful.

Comment.—Even in the presence of an existing diverticulitis, if acute appendicitis cannot be ruled out, an exploratory operation is indicated. If the appendix is not involved and can be removed without danger of fistula formation, it should be done.

CASE 6 (90123).—S. S., a 23-year-old white man, was admitted to the hospital May 2, 1949, complaining of right lower quadrant pain with nausea and vomiting. His past history had been essentially negative. About forty-eight hours before admission he began to have dull pains through the lower abdomen which localized in the right iliac fossa about eighteen hours before admission. He described the pain as continuous and aching. The bowels had moved normally on the day of admission. The abdomen was flat with diffuse muscle spasm and tenderness over the right lower quadrant, the maximum tenderness being at McBurney's point. No mass was palpated. Rectal examination revealed tenderness high on the right side. He had bilateral cryptorchidism. Temperature was 101° F., pulse 100, white blood count 15,000, stabs 4, segmentals 70, lymphocytes 22, monocytes 2. Urine tests showed a trace of albumin, and were negative for sugar. With the above findings a diagnosis of acute appendicitis was made and an immediate operation performed.

The abdomen was open through a McBurney incision and the appendix and cecum visualized. The appendix did not appear to be inflamed although there was some congestion of the serosal vessels. There was a nodular indurated mass the size of a hen's egg palpated in the cecum near the ileocecal valve medially. This mass was very firm in consistency and the differentiation between an inflammatory mass and carcinoma could not be made. No diverticula were demonstrated. Biopsy was not taken because of the danger of fistula formation. Since the patient had not been prepared for resection it was decided to close the abdomen and prepare him for a right colectomy at a later date. One week later, x-ray studies following barium enema were made, with the following report: There was no evidence of diverticulosis or diverticulitis in the colon. The cecum could not be completely filled. The findings were those of a large filling defect in the cecum, the cause of which was not apparent. Certainly a new growth was not ruled out. In view of these findings, the patient was placed on sulfathalidine and streptomycin for four days. A Harrison tube was then placed into the small bowel and on the following day a right colectomy with an end-to-side ileotransverse colostomy was performed through a right rectus muscle-splitting incision. Convalescence was uneventful, and he was discharged on the seventh postoperative day. Pathologic examination showed an inflammatory mass in the cecal wall of probable diverticular origin.

Comment.—Inflammatory lesions of the cecum are usually mistaken for acute appendicitis. The x-ray findings were suggestive of malignancy. In this

case the differentiation could not be ascertained with the abdomen opened, the lesion visualized and palpated. When carcinoma cannot be ruled out, radical resection is indicated. This case of solitary diverticulitis of the cecum brings the total number of cases reported in the literature to date to 102.

SUMMARY AND CONCLUSIONS

1. Surgical interest in colonic diverticulitis was not aroused in this country until 1907, when W. J. Mayo first reported treating five cases by resection of the sigmoid.

2. The etiology is unknown, but the most plausible explanation is an inherent weakness of the muscular walls plus increased intracolonic pressure which results from constitutional or environmental causes.

3. The symptoms of diverticulitis are variable, depending upon the location in the colon, the degree and extent of the inflammatory process.

4. The diagnosis of diverticulitis depends upon the roentgen demonstration of the diverticula. At times the differential diagnosis constitutes a difficult problem that is not solved preoperatively. This is especially true for cecal involvement.

5. It is estimated that between 15 and 20 per cent of the patients with diverticulitis will have complications requiring surgery.

6. The surgical management of diverticulitis has not been ideal. It calls for individualization, good judgment, and patience on the part of the surgeon and the patient.

7. As a general rule, surgery should be reserved for the complications of diverticulitis, namely: acute perforation, abscess, obstruction, fistula formation, coexisting carcinoma, and inability to differentiate diverticulitis and carcinoma.

8. Bowel resection should not be undertaken in the presence of an active inflammatory process.

9. When there is complete obstruction or fistula formation, a colostomy should be made, preferably in the transverse colon proximal to the lesion, and after an optimum waiting period of one year the colostomy may be closed or the involved segment resected, depending upon the condition of the bowel.

10. When carcinoma cannot be ruled out, radical resection is indicated.

11. A review of the literature has been made. The etiology, diagnosis, and surgical management are discussed.

12. Six cases of surgical diverticulitis are reported.

13. Included is one case of solitary cecal diverticulitis bringing the total number reported in the literature to 102.

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BACTERIOLOGIC STUDY OF THE HUMAN LIVER

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THE role of infection in the disastrous consequences of sudden interruption of the hepatic arterial blood supply and in bile peritonitis has long been the subject for discussion.[1] Experimental observations have shown that the normal dog's liver harbors pathogenic anaerobes and that in this animal the free escape of bile into the closed peritoneal cavity incites the development of peritonitis by anaerobic organisms.[2, 3] Clinical experience with human patients would indicate that the observations in dogs cannot be applied to man. In order to study this question more directly, human liver tissue was cultured to observe what, if any, bacterial flora might be obtained.

METHODS

Liver tissue was secured at the time of laparotomy from twelve patients subjected to operation because of malignant neoplasms in the lower abdomen.

The segments of hepatic parenchyma removed weighed 200 to 500 mg. and measured approximately 1 by 1 by 1 cm. This tissue was obtained by the method shown in Fig. 1. After liver biopsy a soft rubber drain was inserted to the biopsy site, brought out through the laparotomy wound, and removed in several days.

The tissue immediately after removal was placed on sterile gauze and divided into approximately equal portions by a clean scalpel. One portion was immediately dropped into a tube of fluid thioglycollate medium,* and the other half into a tube of "purple" (bromcresol purple) milk. These tubes were kept in the incubator at 37.5° C. for three weeks and observed daily for growth. Where growth developed subcultures were made for identification of the organisms. A total of twenty-four cultures was made. The pieces of liver were not macerated prior to inoculation in order to reduce the likelihood of contamination.

The results are tabulated in Table I.

In ten instances all cultures were sterile. Two groups of cultures yielded bacterial growth.

In Patient 3, *Bacillus pyocyaneus* was recovered on the third day. In this patient the same organism was recovered from the bladder urine, secured by sterile catheterization, and from the operative wound. Thus it would appear to be a positive control experiment in this series and not indicative that *B.*

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*Manufactured by Baltimore Biological Laboratories, Baltimore, Md.

pyocyaneus was an organism normally present in human liver. The growth of diphtheroids from the cultures of Patient 12 is interpreted to represent contamination.

In no instances were there postoperative complications due to biopsy of the livers.

TABLE I

PATIENT NUMBER	GROWTH	
	THIOGLYCOLLATE MEDIUM	PURPLE MILK
1	0	0
2	0	0
3	pyocyaneus	pyocyaneus
4	0	0
5	0	0
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0
11	0	0
12	diphtheroids	diphtheroids

DISCUSSION

Gordon-Taylor and Whitly,[4] in a bacteriologic study of fifty-four instances of cholecystitis, concluded that the bacterial flora associated with this condition is similar to that of the intestinal contents and that *Clostridium welchii* is almost always associated with severe acute cholecystitis. This study, as indicated, was associated with the extrahepatic biliary duct system already in a pathologic state and does not permit the inference that a pre-existing hepatic flora of pathogenic organisms is present. The same remark can be made concerning the clinical and experimental studies previously published regarding bacterial studies of the liver associated with acute or marked chronic intestinal obstruction.

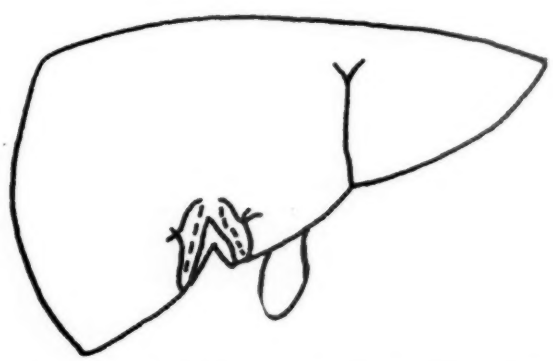

Fig. 1.—Diagram showing the method of securing a small segment of liver for bacteriologic culture at the time of laparotomy. Two compressing mattress sutures of catgut are inserted about a wedge of liver at the anterior margin of the right lobe. The wedge of tissue is excised and the edges then approximated by interrupted sutures (catgut is used). A soft rubber drain is always inserted to the biopsy site.

It would appear, from the observations reported by the writers, that the human liver in the patient not suffering from inflammatory disease of the extrahepatic biliary tract or from acute or marked chronic bowel obstruction

must be regarded as free from viable pathogenic organisms. Possibly, in the presence of a large infected intra-abdominal neoplasm or in the presence of peptic ulceration bacteria could gain entrance into the liver, but in the normal human subject there does not appear to be a "normal" hepatic flora.

CONCLUSIONS

Bacteriologic studies on human liver removed specifically for these studies in the course of operations for lower abdominal cancer indicate that this organ does not normally contain viable bacteria which under certain conditions may become pathogenic.

The authors wish to acknowledge the aid of Dr. Sophie Spitz and Miss Tefta Zograff of the Department of Pathology in connection with the bacterial cultures.

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EFFECTS OF THE LIGATION OF THE HEPATIC ARTERY IN DOGS

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INTRODUCTION

THE liver is unusual in that it is supplied with blood by two routes—the portal vein and the hepatic artery. A great deal is known concerning both the anatomical and functional interrelations of these two afferent blood supplies. Measurements of the volume of flow have indicated that, on the average, the portal vein carries 70 to 80 per cent of the total blood flow to the liver, but Soskin and co-workers[1] and Grindlay, Herrick, and Mann[2] have shown that, in a given animal, wide and usually reciprocal variations may occur rapidly in the ratio between arterial and venous inflow. Values as high as 90 per cent and as low as 10 per cent have been recorded for this ratio.

Studies of the intrahepatic circulation[3, 4] have demonstrated a close relationship between the arterial and venous supplies to the liver. The hepatic artery supplies blood not only to the blood vessels and the biliary passages, the supporting structures and the cells of the hepatic parenchyma, but also to the sinusoids. Portal blood flows directly to the sinusoids. The proportion of the admixture is regulated by inflow sphincters on each type of vessel. Numerous direct arterioportal anastomoses have also been demonstrated in the normal liver.[4]

The complete interruption of portal blood flow by the performance of an Eck's fistula has been shown to result in moderate parenchymal fibrosis and considerable reduction in the size of the liver; but dogs do not die, and little or no alteration occurs in hepatic function.[5]

On the other hand, many investigators have reported that, in the dog, cat, and rabbit, death almost always results following the complete interruption of blood flow in the hepatic artery.[6, 7, 8] Markowitz, Rappaport, and Scott[9, 10] have also reported a high mortality in dogs. But these investigators were the first to demonstrate a practical method of reducing the mortality following complete ligation of the hepatic artery. They have reported that almost all their dogs survived if given very large doses of penicillin after ligation. Furthermore, when the penicillin was discontinued after ten days, the animals did not die. They appeared well when examined three months post-

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operatively. Some seven months after the publication of the first article from Toronto,[9] Davis, Tanturi, and Tarkington[11] reported confirmation of the effects of penicillin.

Obstruction of the hepatic artery has been reported in human subjects in a number of instances. At least thirty cases of accidental or intentional ligation of the hepatic artery have occurred; of these sixteen died.[12, 13, 14] Recently a series of seventy fatal cases has been reviewed,[15] in which death was attributed to infarction of the liver, this in turn being attributed, usually, to obstruction of the hepatic artery caused by embolism, thrombosis, or periarteritis nodosum.

It is evident that the findings of Markowitz, Rappaport, and Scott are of great importance from both the experimental and clinical standpoints.* The results reported in this paper confirm the findings of these authors and indicate, in addition, some of the changes which occur as a result of the complete ligation of the hepatic artery in the dog.

METHODS

The experiments were carried out on apparently healthy, normal dogs of either sex, weighing between 10 and 16 kilograms. In view of the reported toxic effects of meat extractives after liver injury,[16] all the dogs received a meat-free diet ad libitum for a short period preoperatively and for two months postoperatively. The diet contained bread, milk, and sucrose, with suitable additions of mineral salts and brewers' yeast. The caloric intake was distributed in the following way: carbohydrate 65 per cent, protein 15 per cent, and fat 20 per cent.

Haberer[6] has shown that, in order to interrupt completely the arterial flow to the liver by way of the porta hepatis, it is necessary to ligate not only the hepatic artery proper, but also all the arteries with which it anastomoses. Death did not result when the gastroduodenal arch or the right gastric artery was left unligated.

The following technique was used for exposing and ligating the hepatic artery and its branches. To minimize the incidence of incomplete ligation of the vessel, the procedure was followed meticulously. Under intravenous Nembutal anesthesia (35 mg. per kilogram), the hepatoduodenal ligament was exposed through a midline incision, the hepatic artery was ligated at its origin from the celiac artery, and the vessel was drawn to the left and then anteriorly behind the portal vein and bile duct in such a way that it lay to the left of these structures. The vessel was then separated from the surrounding tissues by blunt dissection and heavy linen ligatures were tied along its entire course; one ligature was placed around the terminal branches of the artery as near as possible to the porta hepatis. Ligatures were also placed about the gastro-

*Since this paper went to press, the successful use of antibiotics after ligation of the hepatic artery in human beings has been reported. J. L. Grant, W. T. Fitts, Jr., and Isidor S. Ravdin[33] ligated the hepatic artery for aneurysm in two cases. W. F. Rienhoff, Jr.,[34] ligated the hepatic artery in order to reduce portal hypertension due to intrahepatic block in six patients. He mentions also four patients whose cases were similar, who were operated upon by other surgeons. P. W. Edgecomb and C. Gardner[35] reported a dramatic case of accidental ligation of the hepatic artery distal to the origin of the gastroduodenal and right gastric arteries.

duodenal arch and the right gastric artery. A segment of the portal vein was also completely freed of surrounding tissues. By this technique it was possible to expose and ligate the sheaf of small arteries which arose from the hepatic artery and passed posteriorly and to the right behind the portal vein and the bile duct to the right lobes of the liver (Fig. 1). During dissection, a large number of the hepatic lymphatics and autonomic nerve fibers were unavoidably damaged.

In some animals, "sham ligation" was performed. The exposure dissection and placing of ligatures were carried out as previously described, but the ligatures were not tied and were removed before closure of the abdomen.

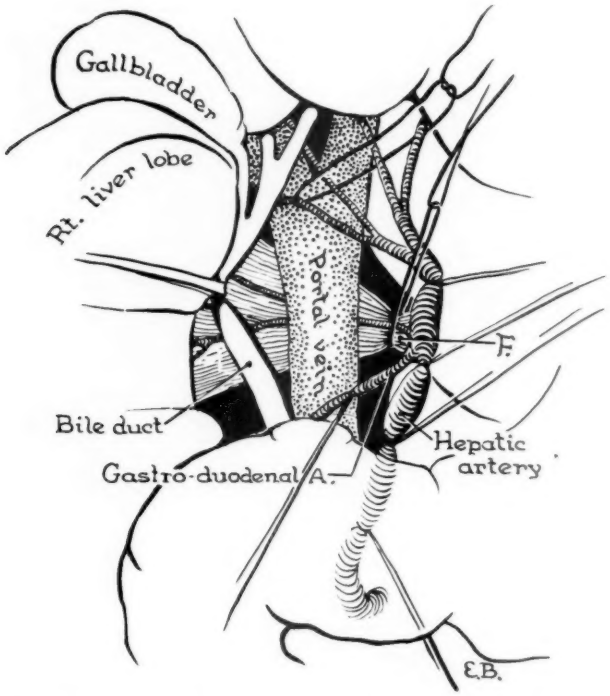


Fig. 1.—The branches of the hepatic artery are prepared and ligatures slung around them. The denuded portal vein overlies a fan of tissue (*F*) containing a sheaf of small arteries.

Complete interruption of blood flow in the hepatic artery was usually verified at the time of autopsy by the intra-aortic injection of liquid latex under a hydrostatic pressure of approximately 80 cm. of water. This material was used to demonstrate collateral arterial supply because it did not pass through the capillary bed into the venous system of the liver, and yet was sufficiently fluid to enter extremely fine arteries.

Liver histology was studied in wedges of tissue taken from the anterior aspect of the diaphragmatic surface of the right and left lobes of the liver, either at biopsy or at autopsy.

Bacteriologic samples were obtained at autopsy by stabbing a sterile swab through a thoroughly seared area of the liver capsule. This technique was

known to have certain limitations but, under the conditions obtaining in the experiment described here, it was impracticable to attempt their elimination. Antibiotic neutralizing agents were not added to the culture media. Bacteriologic and histologic studies, when reported, were made on specimens obtained not longer than twenty minutes after death.

The liver function tests listed in Table I were employed in the present investigation:

TABLE I. LIVER FUNCTION TESTS

TEST	METHOD	MODIFICATION
Thymol turbidity	Maclagan[17]	Thymol reagent buffered at pH 7.55[18]
Bromsulfalein excretion	Rosenthal and White[19]	Bromsulfalein 10 mg. per kg. IV[20]
		Retention measured at 560 μ: 15 min. (and usually 30 min.) after injection
		20 mg. bromsulfalein per 100 ml. plasma considered as 100 per cent retention
Plasma bilirubin (direct and total)	Malloy and Evelyn[21]	Schiff[22]
Serum proteins	Fractionation: Campbell and Hanna[23]	
	Protein determination: Gornall, Bardawill, and David[24]	
Urinary urobilin (qual.)	Schlesinger[25]	
Urinary bilirubin (qual.)	Harrison[26]	

One group of the dogs studied in the present investigation received no antibiotic therapy. A second group received 100,000 units of crystalline potassium penicillin G intraperitoneally and 300,000 units of procaine penicillin G in oil intramuscularly at the time of ligation. This dosage was repeated once daily for nine or ten days, then discontinued. A third group received a combination of antibiotics. The administration commenced several hours prior to the ligation of the hepatic artery, and was continued for ten days postoperatively. The animals received the following dosages of antibiotics daily:

Procaine penicillin G in oil, 300,000 units intramuscularly × 1.
Crystalline potassium penicillin G, 66,000 units intramuscularly × 3.
Dihydrostreptomycin, 0.25 Gm. intramuscularly × 2.
Chloromycetin, 0.08 Gm. orally × 3.
Sulfamerazine, 0.4 Gm. orally × 3.

Gas-gangrene antitoxin, active against the toxins of *Clostridium welchii,* vibrion septique, and *Clostridium oedematiens,* was administered, one injection being given preoperatively and one twenty-four hours postoperatively.

DESIGN OF THE INVESTIGATION

The experiments reported here were carried out with two main objectives. The first was to repeat the experiment described by Markowitz, Rappaport, and Scott,[10] who reported that the mortality of dogs following complete liga-

tion of the hepatic artery was greatly reduced by intensive penicillin therapy. The second was to investigate in detail certain changes taking place in the liver of dogs that had undergone this operation.

Three groups of dogs were studied in the present investigation:

(1) A group of eleven dogs in which the hepatic artery was ligated, but in which no antibiotics were administered;
(2) A group of twenty dogs in which the hepatic artery was ligated and antibiotics were administered for ten days postoperatively, fourteen receiving penicillin only, six receiving a combination of antibiotics;
(3) A group of six sham-ligated dogs in which the hepatic artery was not tied.

The mortality rate for each group was determined. Whenever possible, histologic and bacteriologic studies were carried out on the livers at the time of death. During the period following ligation of the hepatic artery, an evaluation of the hepatic function was repeatedly made when possible. For the purpose of recording mortality, dogs were not considered to have survived ligation until definite evidence of disturbed hepatic function was no longer present. After this period, liver biopsies were performed. Six of the penicillin-treated dogs that survived were investigated for a total period ranging from three to six months. At the time of sacrifice, terminal histologic studies were carried out.

EXPERIMENTAL RESULTS

Mortality.—The hepatic artery was ligated in eleven dogs which did not receive antibiotics. Ten died—a mortality rate of approximately 90 per cent.

On the other hand, of the twenty dogs which received antibiotic therapy for ten days after ligation of the hepatic artery, all but seven survived—a mortality rate of approximately 35 per cent. The mortality data were subjected to the χ 2 test of significance and the reduction in mortality observed in the antibiotic-treated dogs was significant at the 1 per cent level. Of the group of six dogs that received the combination of antibiotics, two died. Hence, the mortality rate was not different from that of fourteen dogs that received penicillin only.

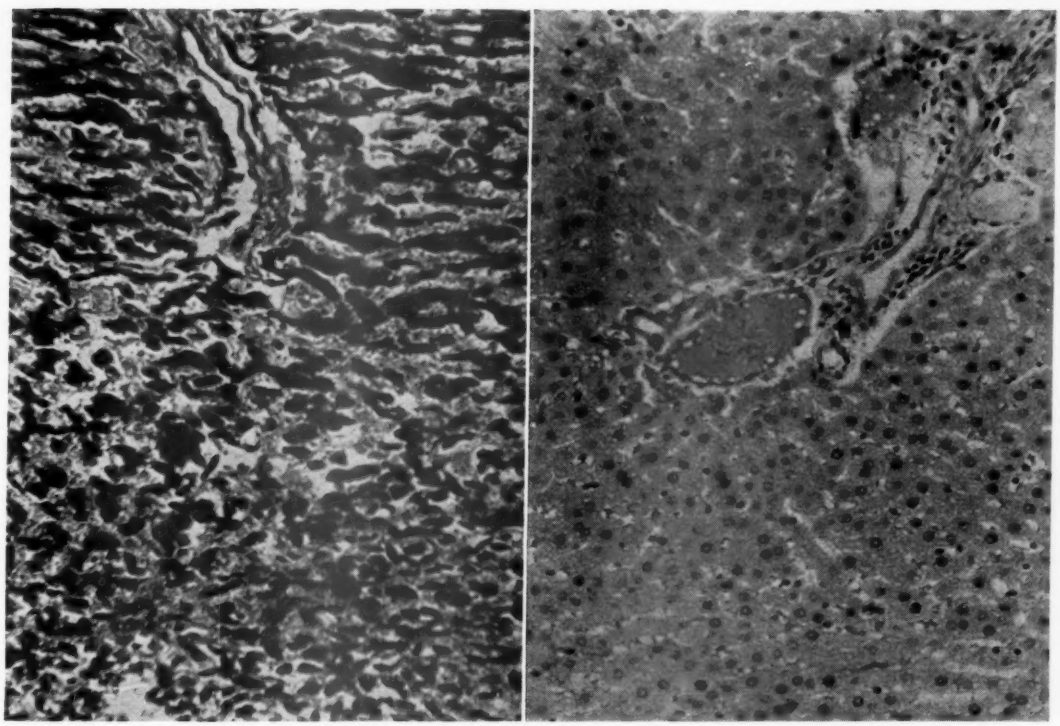
Of the six dogs upon which a sham ligation had been performed, none died.

Observations Made Upon Dogs Not Receiving Antibiotic Therapy Following Ligation of Hepatic Artery.—Of eleven dogs to which no antibiotic therapy was administered following ligation of the hepatic artery, ten died. Death occurred as early as eighteen hours and as late as six days postoperatively, the average period of survival being fifty hours.

The gross appearance of the liver was abnormal in all the dogs that died. The lesion varied from irregular mottling or sloughing of the capsule with softening of liver parenchyma, to a lesion in which large amounts of liver parenchyma had become pale and friable, and in which the entire liver substance had become softened and sometimes crepitant. Occasionally, discrete

abscesses were observed. The gall bladder wall had become softened and edematous in every instance, and in each of the three animals which survived longer than two days, the gall bladder had perforated prior to death.

Only in six dogs was it possible to obtain satisfactory histologic and bacteriologic data at the time of death. In these, necrosis was invariably observed in sections. The less severe lesions took the form of atrophy, dissociation and necrosis of hepatic cells, usually centrilobular in distribution. However, in most cases, the necrotic lesion consisted of marked or complete cell lysis which had spread to involve the entire lobule (Fig. 2). In more than half the animals in this series, the damage appeared most severe in the left part of the liver. This finding remains unexplained.



A. *B.*

Fig. 2.—Photomicrographs of paraffin sections of liver biopsies taken twenty-four hours postoperatively: *A*, Complete cell necrosis after ligation of the hepatic artery without penicillin treatment. *B*, Almost normal histology after ligation of the hepatic artery, treated with penicillin.

Only one dog in this group survived. The animal appeared to be reasonably well by the tenth day, at which time it was sacrificed. Although the right half of the liver appeared to be normal on gross examination, the left contained many medium-sized unresolved abscesses from which *Clostridium welchii, Bacillus coli* and *Streptococcus haemolyticus* were isolated. The necrotic and ruptured gall bladder was walled off by adhesions. We cannot predict what would have been the fate of this animal, had it not been sacrificed.

Bacteria were isolated from the liver parenchyma of all the dogs investigated, and aggregations of bacteria were visible in histologic sections in four.

As judged by cultural, morphological and tinctorial criteria, a variety of organisms appeared to be involved. Frequently, the aggregations of bacteria seen in the necrotic regions were of more than one type (Fig. 3). Representatives of the clostridia, the gram-positive cocci, and the gram-negative coliform bacilli were encountered.

These results were in marked contrast to the findings of similar investigations in ten apparently normal dogs. Positive cultures were obtained in only 30 per cent of these and aggregations of bacteria were not demonstrable in any instance.

Because of the short survival period evaluation of hepatic function could not be made in dogs that did not receive antibiotic therapy.

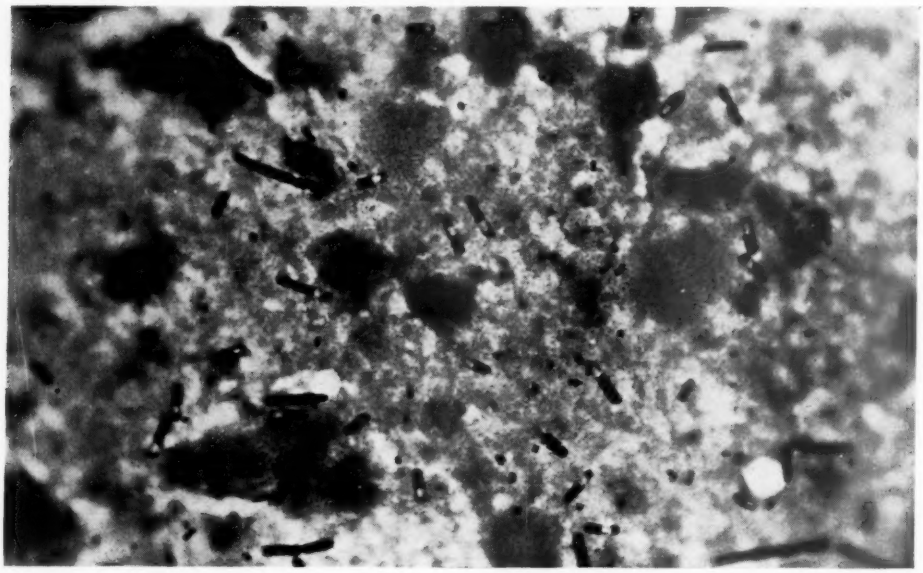


Fig. 3.—Variety of microorganisms in necrotic liver tissue. Some are spore-bearing.

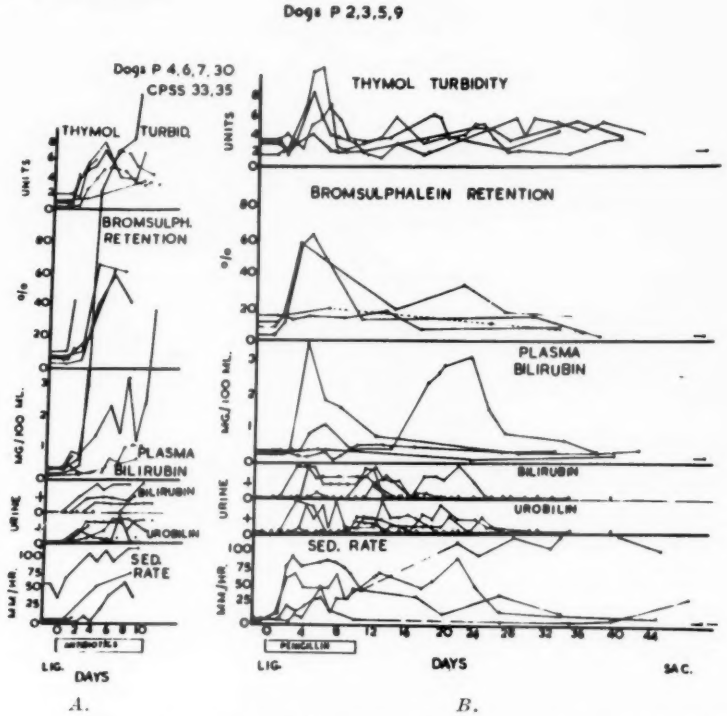
Observations Made Upon Dogs Receiving Antibiotics Following Ligation of Hepatic Artery.—Antibiotic therapy was shown to reduce greatly the mortality following ligation of the hepatic artery, because, of the twenty dogs receiving this treatment, all but seven survived. The efficacy of antibiotic therapy indicated that bacterial proliferation was an important factor in causing death after ligation of the hepatic artery.

However, the death of the seven dogs that died despite antibiotic therapy needs an explanation. In all these dogs the gall bladders were necrotic due to the ligation of the cystic artery. Three showed frank perforation and bile peritonitis, the remaining four had the necrotic gall bladders walled off by adjacent viscera which adhered. Nevertheless, the livers of all the dogs showed various degrees of necrotic and postnecrotic lesions which suggest the possibility of an anemic necrosis.

Bacteriologic examinations were carried out in six of the seven antibiotic-treated dogs that died. Cultures were negative in four, and positive in two

dogs in which the gall bladder had a frank perforation. Bacteria could not be demonstrated in sections of necrotic liver in five of the dogs, but were present in one of the animals in which perforation of the gall bladder had occurred. The findings suggested that, in four of these six dogs which died despite antibiotic therapy, bacteria did not play a role in the production of the widespread hepatic necrosis observed in each instance.

The results of the bacteriologic studies, made on antibiotic-treated dogs that died, differed very greatly from similar studies carried out on dogs that received no antibiotics. In the latter animals, bacteria were invariably demonstrated. Of the seven antibiotic-treated dogs that died, two had received a combination of several antibiotics. The clinical, pathologic and bacteriologic findings were indistinguishable from those made on dogs that had received penicillin only. Thirteen of the twenty dogs that received antibiotic therapy survived ligation of the hepatic artery. Nine received penicillin, four a combination of antibiotics.

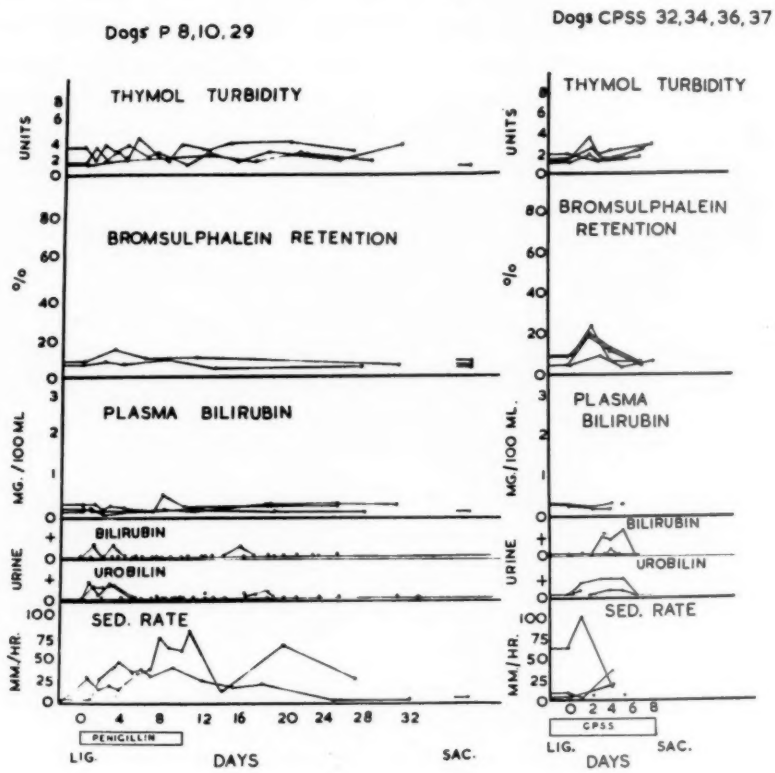


A. *B.*

Fig. 4.—Liver function tests: *A*, Severe disturbance of liver function, leading to a fatal outcome. *B*, Severe but transitory hepatic insufficiency lasting in some cases as long as six weeks, and showing recurrence in others.

The study of mortality precluded the study of histologic alterations in liver morphology during the period immediately following interruption of blood flow in the hepatic artery. However, a correlation was made of the changes occurring in the liver function tests during the early postoperative period, and the histologic changes observed in the liver from four to six weeks postoperatively, after which time survival was considered to be assured. In this manner an indication was obtained of the effects resulting from ligation in penicillin-treated dogs that survived.

The alterations observed in the liver function tests enumerated earlier are indicated in Fig. 4. On the basis of these tests, it was possible to classify the nine surviving penicillin-treated dogs into three groups. In one group of three dogs there was a very severe but transitory period of hepatic insufficiency (Fig. 4, *B*). The occurrence of marked parenchymal damage was indicated by an abrupt elevation in the values of the thymol turbidity test, the bromsulfalein retention test at fifteen minutes, and the direct plasma bilirubin level, and by the appearance of large amounts of urinary bilirubin and



A. *B.*

Fig. 5.—Dogs given (*A*) penicillin, or (*B*) the antibiotic mixture, postoperatively. All show normal liver function tests.

urobilin. Abnormalities first became evident on the second or third postoperative day, and reached a maximum by the fourth day. The rapidity of onset and the intensity of the functional disturbance were comparable with the changes observed in animals that did not survive (Fig. 4, *A*). However, all the hepatic function tests had become normal, or almost normal, by the twelfth postoperative day.

In the remaining group of three dogs, no liver dysfunction was observed at any time (Fig. 5, *A*).

To generalize, it may be said that, in considering the group of nine penicillin-treated dogs that survived ligation, a disturbance in liver function occurred in two-thirds of the group within a few days of operation, and that

all evidence of frank hepatic insufficiency had disappeared by the time penicillin therapy was discontinued on the twelfth postoperative day.

However, in four of the dogs, recovery was not permanent, and disturbance in the liver function tests recurred (Fig. 4, *B*). The secondary hepatic insufficiency was usually less severe than initially. The disturbance had become evident by the sixteenth day in each case, and varied in duration from two days to three weeks. In two dogs there was persistence of a slight elevation in the thymol turbidity test for as long as six weeks postoperatively.

Liver biopsies were carried out in each of the nine surviving penicillin-treated dogs between four and six weeks after ligation of the hepatic artery. In general, the morphologic changes observed corresponded with the various changes noted earlier in liver function. In six dogs, structural changes were noted at this time. In two, unresolved abscesses were present in the left lobes, but in the remaining four the changes were not visible in the gross, and

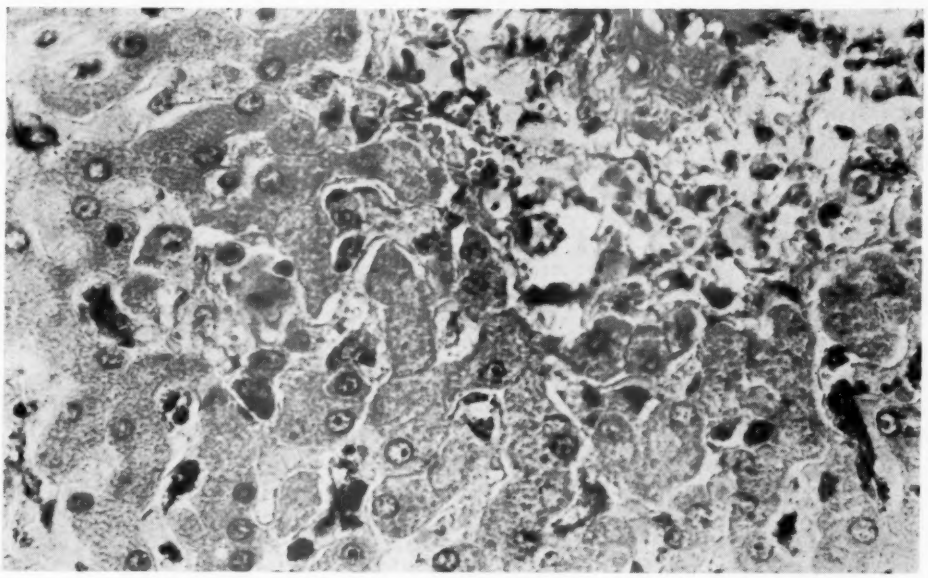


Fig. 6.—Shrunken parenchymal cells, some containing iron pigment. The reticulin fibers appear collapsed.

necrosis was not present. The lesions observed on microscopic examination were usually centrilobular but were occasionally periportal. In the centrilobular regions there was a considerable reduction in the size and number of the parenchymal cells of the liver, and the shrunken cells which remained usually contained iron pigment which was suggestive of earlier hemorrhage (Fig. 6). The supporting reticulin fibers appeared to have collapsed about the central veins. These findings suggested earlier centrilobular necrosis which had become resolved.

In three dogs that survived, no gross or microscopic abnormalities were observed in the liver parenchyma.

The gall bladder appeared normal in one dog, was atrophic in one, and had completely disappeared in the remaining seven dogs.

Six of the penicillin-treated dogs that survived were observed for a total postoperative period ranging from three to six months. No late development of hepatic insufficiency was observed in any of these animals. At autopsy, the total size of the liver appeared normal, but in four of the six dogs a very marked reduction had occurred in the size of the left lobe, the remaining lobes having undergone compensatory hypertrophy. The explanation of this atrophy was not evident; it was not correlated directly with changes observed earlier at the time of biopsy.

Examination of the relatively small volume of damaged liver indicated that there was a very marked centrilobular fibrosis with extensive parenchymal atrophy in these regions (Fig. 7). In the remaining portions of the liver, there was no gross or microscopic evidence of abnormality in any of the dogs. The signs of necrosis and atrophy that had been noted earlier at biopsy were no longer visible, except occasionally increased periportal fibrosis. The deposition of fibrous tissue is illustrated in Fig. 8, *B*.

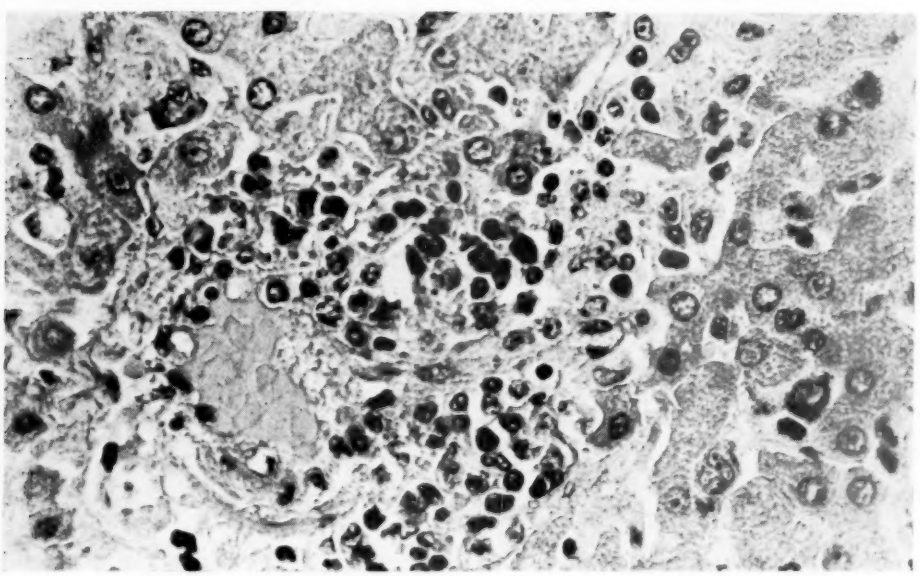


Fig. 7.—Centrilobular fibrosis and parenchymal atrophy.

The observations made upon penicillin-treated animals had indicated that this antibiotic did not prevent death in all dogs after ligation of the hepatic artery, and further, that penicillin-treated dogs that survived ligation frequently developed a transitory hepatic lesion a short time postoperatively. In order to determine whether these effects could be prevented by increasing the effective range of antibiosis, a combination of several antibiotics was administered. As described earlier, the dogs received penicillin, streptomycin, chloromycetin, sulfamerazine and gas-gangrene antitoxin. In order to establish effective concentrations of antibiotics at the actual time of operation these drugs were administered some hours prior to ligation of the hepatic artery, and suitable doses were administered thereafter until animals died or were sacrificed.

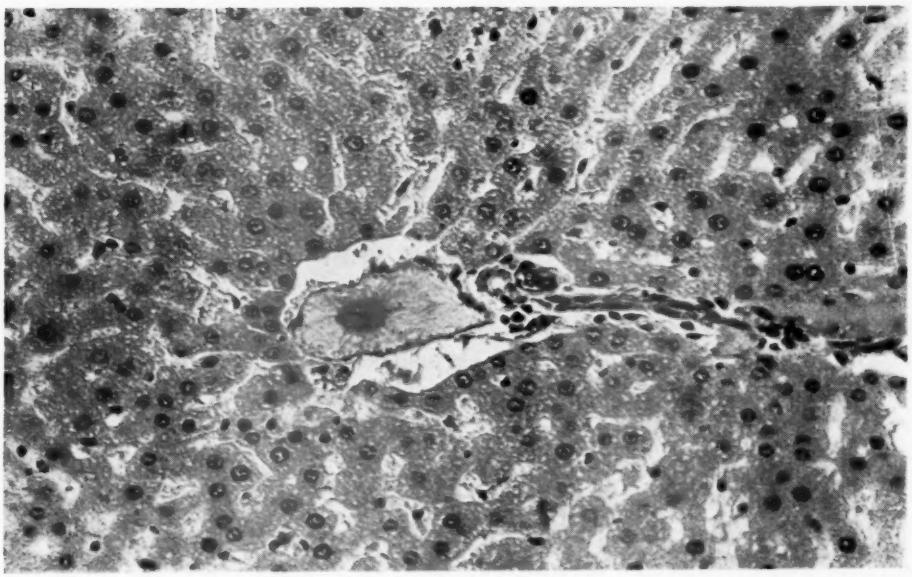


Fig. 8, *A*.—Normal portal area.

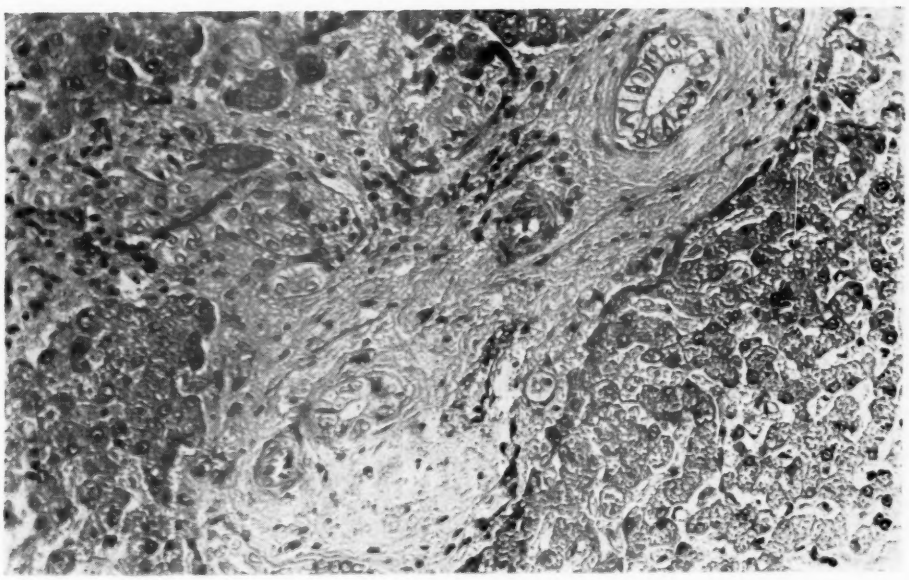


Fig. 8, *B*.—Periportal fibrosis six months after ligation of the hepatic artery.

Six dogs received this treatment. Of these, two died, one on the second postoperative day and one on the ninth. As noted previously, the widespread necrosis and severe hepatic insufficiency were as marked in these two dogs as in the five penicillin-treated dogs that died.

On the other hand, the alteration observed in hepatic function of the four dogs that survived was not so severe as that which occurred in the surviving dogs that received only penicillin (Fig. 5, *B*). In no instance did a significant rise occur in the thymol turbidity test nor in the plasma bilirubin concentration. The changes were limited to transitory slight elevations in bromsulfalein retention and in urinary bilirubin and urobilin. However, the small series makes interpretation of the findings difficult.

Liver function tests were normal by the tenth day in the four dogs that survived, and they were sacrificed at this time. The gall bladder and a small portion of adjacent liver tissue were necrotic in three dogs. However, there was no histologic evidence of damage in the remaining liver parenchyma and little or no inflammatory reaction was present in any of the livers.

Bacteriologic studies were made in each of the animals that received the combination of antibiotics. Bacteria were not demonstrated in tissue sections or in cultures of the liver or gall bladder, and in every case even necrotic areas were free of demonstrable bacteria.

Observations Made on Penicillin-treated Dogs Upon Which Sham Ligation Was Performed.—There was no mortality in the six dogs upon which sham ligation was performed. In four of them, no abnormalities were detected in liver function or histology; minimal or transitory late changes appeared in two. Hence, the marked alterations frequently observed after complete ligation of the hepatic artery were considered to be specifically attributable to interruption of blood flow in this vessel.

Latex Injections.—Latex injection of the residual arterial supply to the liver was undertaken at the time of death for two purposes: (1) to verify the completeness of the earlier ligation of the hepatic artery and its branches, and (2) to obtain a qualitative estimate of the amount of arterial blood entering the liver at the time of death.

A study of the arterial blood supply of normal dogs indicated that, in addition to its supply from the hepatic artery, the liver invariably received a small amount of arterial blood by way of collateral routes. From two to five vessels entered the liver as branches of the right and left phrenic arteries, which formed an anastomotic arch upon the inferior surface of the diaphragm immediately anterior to the hiatus of the inferior vena cava. In addition, one or sometimes two branches entered the left lobe of the liver from the left gastric artery, and a small arterial plexus surrounding the structures in the hepatoduodenal ligament usually extended as far as the porta hepatis. The caliber of each of these vessels was extremely small in normal animals, the diameter being similar to that of a hair. Thus, the total collateral arterial supply was very small under normal circumstances.

Latex injection was carried out in eight of the antibiotic-treated dogs that survived. Complete obstruction of the hepatic artery was confirmed in

six. In the remaining two, the arterial supply in the hepatoduodenal ligament was greatly reduced but not completely obstructed. In every instance, the collateral arterial vessels had increased in number, and the diameter had increased to that of a fairly coarse thread. A similar result has been reported by Bollman,[27] in dogs that survived ligation of the hepatic artery.

Latex injection was carried out in three antibiotic-treated dogs that developed massive hepatic necrosis and died between eight and eleven days postoperatively. During this period the collateral arterial supply appeared to have become hypertrophied to an extent comparable with that of dogs that survived.

DISCUSSION

The results obtained in this experiment confirmed the earlier findings of Markowitz and co-workers.[9, 10] Complete ligation of the hepatic artery resulted in a septic hepatic necrosis which was nearly always fatal. On the other hand, the administration of antibiotics reduced the mortality from ligation of the hepatic artery to approximately 35 per cent and, although penicillin was discontinued on the tenth postoperative day, the dogs did not subsequently develop hepatic insufficiency when observed for as long as six months. The improvement in the survival rate following the use of antibiotics was statistically significant and indicated the importance of bacteria in determining the fatal outcome following interruption of blood flow in the hepatic artery.

Incomplete ligation of the hepatic artery was not responsible for the improvement in the survival rate, since it was established by intra-arterial Latex injection, that the hepatic artery had been completely interrupted in six of the eight surviving animals that were investigated at autopsy. In the other two the arterial blood supply was greatly reduced.

Of the twenty dogs studied, seven died after obstruction of the hepatic artery despite the administration of antibiotics. Generalized bile peritonitis occurred in two, localized bile peritonitis in one. But it was impossible to demonstrate bacteria either in sections of, or in cultures from, the necrotic lesions of the liver in four of the remaining six dogs. It therefore appeared probable that, in these four dogs, ligation of the hepatic artery had produced a fatal aseptic ischemic necrosis.

Failure to culture bacteria from certain of the necrotic livers in antibiotic-treated dogs was not considered to be attributable to the absence of antibiotic-neutralizing agents from the culture media. It is reasonable to postulate that the concentration of antibiotics present in vivo would exert a greater bacteriostatic effect on the bacteria in the liver than would the much lower concentration of the same antibiotics which had been transferred to the culture medium by means of the sampling swab.

Studies carried out upon penicillin-treated dogs that survived also indicated that frequently penicillin did not entirely prevent hepatic necrosis. Liver function studies and histologic examination suggested that a necrotic lesion, usually centrilobular in distribution, developed postoperatively in more

than half the dogs that survived, but that this necrosis was transitory. Similar marked disturbances in liver function and morphology were not observed in six sham-ligated dogs, indicating that these effects were not directly attributable to operative manipulations and injury to structures other than the hepatic artery. Markowitz and co-workers[10] suggested that the hepatic necrosis which developed after ligation of the hepatic artery was primarily caused by the anaerobic proliferation of organisms similar to *Clostridium welchii*, which, in turn, caused destruction of liver cells. They believed that, by preventing this proliferation, parenchymal necrosis could be prevented. However, our findings suggest that an aseptic hepatic necrosis may result from ligation of the hepatic artery in dogs adequately treated with antibiotic agents. This, therefore, supports the suggestion that, in the absence of antibiotic therapy, the fulminating bacterial proliferation may be secondary to an antecedent ischemic parenchymal necrosis which constitutes the primary, though not necessarily the fatal, lesion.

A number of authors[28, 29, 30] have reported the frequent isolation of bacteria from the livers of normal animals. Therefore, it is conceivable that the necrotic liver parenchyma forms a suitable locus for their proliferation. Recently Lewis and Wangensteen[36] demonstrated rod-shaped, gas-forming bacteria in pieces of dog's liver left free in the peritoneal cavity of the animal. All of their animals not treated with penicillin died with peritonitis. Of the dogs in the penicillin-treated group, only three out of the twelve died. Studies of the cultural, morphologic and tinctorial characteristics of the bacteria isolated from the necrotic lesions of animals that did not receive antibiotic therapy indicate that a variety of microorganisms may be associated with the necrotic process.

The role of bacteria in the production of the lesions seen in dogs that survived ligation of the hepatic artery is not yet fully established. The substitution of several antibiotic agents for treatment with penicillin alone did not improve the incidence of survival in a small series of dogs. Fitts, Scott, and Mackie[33] report the prevention of hepatic necrosis in dogs by parenteral treatment with aureomycin, given for five days postoperatively. However, the recurrence of hepatic insufficiency after discontinuance of penicillin therapy and the reduction in the incidence and severity of hepatic lesions in dogs which received a combination of antibiotics suggest that bacteria played an important part in producing these transitory lesions. From the evidence available at present, it would seem advisable to administer in correspondingly high dosages a combination of antibiotics with a wide range of antibacterial action in the treatment of clinical emergencies resulting from damage to the hepatic artery.

The nature of the compensatory mechanisms taking place in dogs that survive ligation of the hepatic artery has not been fully investigated. That it was possible to discontinue penicillin ten days after ligation suggests that the compensatory process must have been well advanced within that period. The observed enlargement in caliber and increase in number of the collateral

arterial vessels to the liver is considered to be at least one of the factors. To date, the increase in this collateral flow has not been measured quantitatively, nor have measurements been made to determine what changes occur postoperatively in the oxygen tension of the blood leaving the liver by the hepatic veins.

Evidence has been presented which indicates that the hepatic necrosis developing after ligation of the hepatic artery was principally the result of reduced arterial blood supply and of bacterial proliferation. However, one must consider the possibility that two secondary factors may be of importance: (1) postoperative shock with consequent reduction of portal blood flow in an organ already deprived of arterial blood, and (2) possible hepatoxic action of the drugs used in the course of the experiments. With regard to the latter factor, the literature surveyed indicates that the various antibiotic agents have little toxic action on the normal liver.

Similarly, Nembutal in therapeutic doses, although principally inactivated by the liver, produces no demonstrable effect on liver function in the normal dog.[31] The possibility of a toxic action in the damaged liver should, however, be considered.

The interesting report of Tanturi and co-workers[32] has just appeared. This group in an earlier article[11] was the first to confirm the findings of Markowitz, Rappaport, and Scott.[9] In this second paper new light is shed on the mechanisms by which liver necrosis is produced when the branches of the proper hepatic artery are ligated in dogs. They found the enzyme lecithinase, identical with the alpha toxin of *Clostridium perfringens* type A, increased, as a result of bacterial proliferation in the dearterialized liver.

Most of their other findings are similar to ours. They differ in the statement that some of the dogs survived the ligation of the hepatic artery without any antibiotic treatment, and explain this event by "seasonal variation in resistance." This difference in results may, perhaps, be due to different technical factors. Using the common technique of post-mortem injection of the liver vessels with Latex through the aorta and following the channels of collateral blood flow, we were always able to demonstrate collaterals, both in normal dogs and in those in whom the hepatic artery was ligated. Indeed, most of the investigators in this field since, and even before, Haberer's[6] paper report the same fact. On the other hand, we never observed recanalization of the ligated arteries. The coarse, heavy Irish linen thread we use in ligating the common hepatic, gastroduodenal, and hepatic proper branches induces a thick fibrous scarring that can easily be palpated in the hepatoduodenal ligament at autopsy. It constricts the vessels completely.

SUMMARY AND CONCLUSIONS

1. The hepatic artery was ligated in thirty-one normal dogs; twenty received postoperative antibiotic therapy for ten days, eleven did not receive antibiotics. The antibiotic therapy reduced the mortality rate after ligation of the hepatic artery from 90 per cent to 35 per cent.

2. Both bacterial proliferation and reduced arterial blood supply were important factors in causing hepatic necrosis and death following ligation of the hepatic artery. The evidence suggested that a variety of microorganisms might be implicated in the former factor.

3. A number of dogs died despite intensive antibiotic therapy. Hepatic necrosis was present, and, in some of the dogs, there was evidence to suggest that death had resulted from an ischemic necrosis which had developed despite complete suppression of bacterial proliferation by the administration of the antibiotic agents.

4. In a small group of dogs which received a combination of antibiotics both before and after ligation of the hepatic artery, the mortality rate did not differ from that of the dogs receiving penicillin only.

5. Although penicillin therapy greatly reduced the mortality following ligation of the hepatic artery, there was strong evidence that a hepatic necrosis occurred postoperatively in more than half the survivors. In these, however, the lesion was transitory and despite discontinuance of penicillin therapy, no subsequent development of hepatic insufficiency was observable.

6. A small, fairly constant increase in collateral arterial circulation to the liver was observed in all animals examined. This was considered to be at least one of the compensatory changes which occurred during the ten day period following complete obstruction of the hepatic artery.

7. Liver function tests were carried out in the dogs treated with antibiotics. Two-thirds of the dogs, after a transient liver insufficiency, showed normal liver function tests on the twelfth day after operation. In a group of four dogs the liver insufficiency recurred to a slighter degree and lasted from two days to three weeks.

We are grateful to Professor C. H. Best for his guidance and encouragement throughout this investigation, to Dr. A. G. Gornall and Dr. C. J. Bardawill of the Department of Pathological Chemistry, and to the members of the Department of Bacteriology who aided in various aspects of this study. The histopathologic examinations and the photomicrographs were kindly made by Dr. W. Stanley Hartroft.

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PARTIAL HEPATECTOMY IN THE DOG

An Experimental Study

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DESPITE a growing interest in the problem, the liver remains one of the most surgically inaccessible of all the organs. This is partially due to its extreme vascularity and our relatively unsatisfactory methods of hepatic hemostasis. This deficiency is apparent in the established but often fruitless methods of controlling hemorrhage from the hepatic parenchyma in patients with severe traumatic lacerations of that organ.[1, 2] All too frequently, fear of hemorrhage discourages attempts to eradicate primary or metastatic tumors of the liver which would otherwise be amenable to surgical extirpation.

The left lobe, because of its small size and relative accessibility, may be approached fairly readily in human patients by existing methods.[3] The approach to the right lobe is more formidable. The few courageous surgeons[4, 5, 6] who have definitively attacked major lesions in this area have minimized blood loss by rapid operative technique, complete occlusion of the blood supply for short periods of time, or by the utilization of cautery excision or strangulating mattress sutures in the hepatic parenchyma. These measures, although partially successful, are not completely consistent with good surgical principles and are not entirely satisfactory when large lesions are present.

Because it derives its primary blood supply from two sources, the hepatic artery and the portal vein, the liver presents special problems and opportunities for central hemostasis.

Studies seeking to evaluate the effect of ligation of the hepatic artery alone in different species of experimental animals have produced variable results and survival is seemingly dependent upon two factors, the presence of accessory or anomalous arteries[7] and the administration of antibiotics. Markowitz and co-workers[8] first showed that, whereas ligation of the hepatic artery was formerly uniformly fatal in dogs, death may be averted by the administration of massive doses of penicillin. Aureomycin has been found to be similarly effective.[9] These antibiotics serve to inhibit the growth of *Clostridium welchii* type organisms which normally inhabit the canine liver and produce death from overwhelming sepsis when the oxygen tension of the liver is reduced.

The effect of ligation of the hepatic artery in the human being has also been unpredictable in the past and survival, when it did occur, was attributed to the presence of accessory arteries supplying the liver.[10] Berman[11] has recently reported survival of three patients following the definitive ligation of both the hepatic and splenic arteries in the management of portal hypertension. Gurd and co-workers[12] have reported an isolated patient who survived ligation of the hepatic artery during gastric resection. These patients were protected by antibiotics.

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When the portal blood flow is embarrassed, the physiologic effects of portal stasis and of decreased effective systemic blood volume must be considered in addition to those of reduced hepatic blood supply. Eck demonstrated in 1877 that dogs can survive if the liver is deprived completely of portal blood by shunting it into the systemic circulation and many techniques have since been devised for accomplishing portacaval anastomosis in experimental animals and human beings. It has been observed repeatedly, however, that sudden complete occlusion of the portal vein in dogs uniformly results in rapid death. Elman and Cole[13] have shown that death, which eventuates after approximately one hour of complete occlusion, is due to shock incident to the pooling of blood in the portal bed and that death can be delayed, but not prevented, if the systemic blood volume is maintained. This may be accomplished by blood transfusions or by impeding the arterial inflow into the portal bed by simultaneously occluding the celiac vessels. On the other hand, if the portal occlusion is accomplished gradually over several months' time by various techniques, thereby enabling collateral channels to develop spontaneously, the animals survive ultimate complete occlusion.[14]

Rous and Larimore[15] studied the effect of ligation of isolated branches of the portal vein and found that, although the animals survive, atrophy of the liver develops in those segments deprived of portal blood. The remainder of the liver compensates by undergoing hypertrophy provided there has been no interference with the extrahepatic bile ducts and that the arterial supply to the segment is intact.[16] Fishback[17] demonstrated that after partial hepatectomy in the dog maximum hypertrophy of the remaining liver is reached within two months' time.

The most bothersome bleeding encountered following incision into the liver parenchyma is the generalized ooze derived from the portal system, which has been shown to contribute approximately 80 per cent of the total hepatic blood flow.[7] This blood loss may be readily controlled by central occlusion of the portal vein itself. Raffucci,[18] in studying the same problem, has found, however, that it is unsafe to occlude the vascular structures in the hepatoduodenal ligament of the dog for longer than twenty minutes. Wangensteen[19] has observed that it may be unwise to maintain complete occlusion of this type in surgical patients for longer than a few moments at a time.

In planning surgical resections of large masses of hepatic parenchyma, it appears highly desirable to maintain portal blood flow in some fashion. The possibility exists of establishing a portacaval anastomosis as a preliminary measure. This is in itself a formidable procedure and not without profound physiologic disturbances. A more rational approach would appear to be the temporary or permanent occlusion of only those branches of the portal vein which supply the involved segment, leaving the remainder patent to carry the entire portal blood flow. Viability of this involved segment may be anticipated if the arterial blood supply is maintained postoperatively.

This study was undertaken in an effort to evaluate the effect upon the experimental animal of segmentally occluding the portal blood supply to major

segments of the liver during partial hepatectomy, both singly and in conjunction with simultaneous but temporary occlusion of the arterial supply. Our primary aim has been to acquire information which might aid in the development of an operative approach permitting a definitive and unhurried attack upon surgical lesions in the right lobe of the liver in surgical patients.

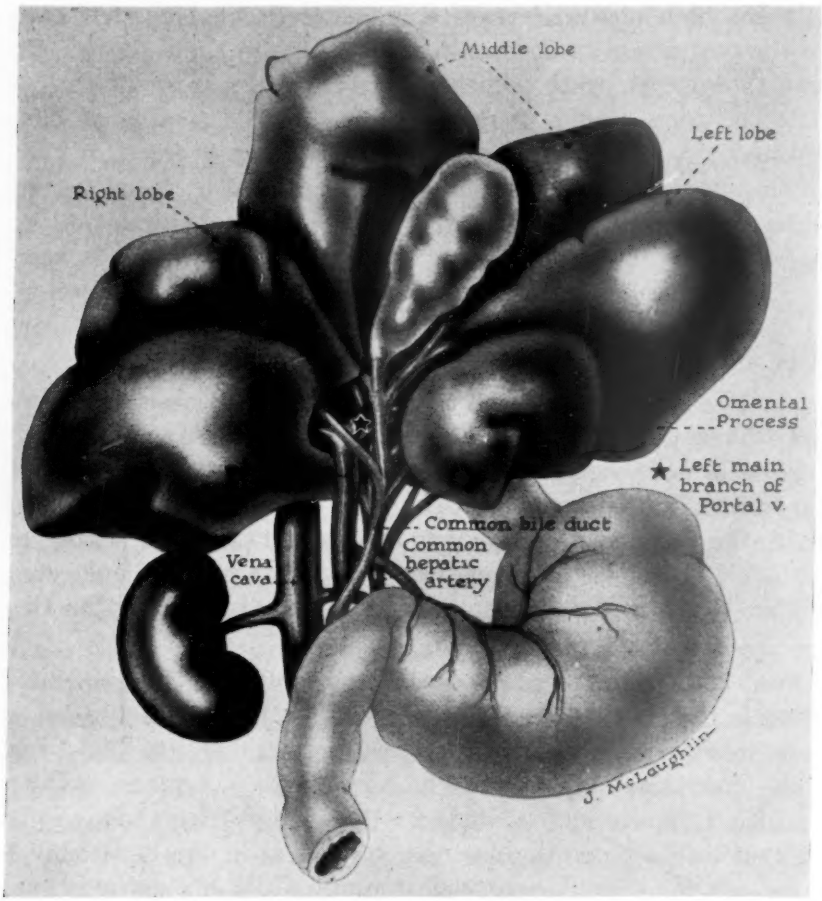

Fig. 1.—Anatomic relations of dog's liver.

ANATOMICAL CONSIDERATIONS

The liver of the dog is divided into three primary lobes, a central or middle which harbors the gall bladder, a right lateral, and a left lateral (Fig. 1). The middle lobe is usually the largest. The right lateral is the smallest, being approximately proportional in size to the left lobe in the human being. The middle and left lateral lobes combined represent 65 to 70 per cent of the total hepatic mass in the average dog[20] and collectively are approximately proportional in size to the right lobe in the human being. The portal vein branches in such a way that the branch to the right lobe leaves the main trunk most caudally. A common trunk thus supplies the middle and left lateral lobe. It is a relatively easy matter to occlude the branch to the middle and left lateral lobes, leaving

the branch to the right lateral lobe intact. In respect to the amount of liver parenchyma deprived of portal blood, this is analogous to occluding the right branch in the human being and permitting all of the portal blood to flow through the left lobe. The duct system overlies the portal vein and must be carefully retracted in approaching the bifurcation of the portal vein. The hepatic artery lies behind and medial to the portal vein, and the main trunk may be approached with relative ease.

PLAN OF STUDY

Thirteen mongrel dogs varying in weight from 11.5 to 23.5 kilograms were utilized. They received no special dietary preparation. Liver function studies were obtained preoperatively and at intervals postoperatively. These consisted of determinations of bromsulfalein clearance and serum bilirubin (which Hoffbauer[21] found reflected the state of the liver in the dog better than other laboratory studies) as well as serum protein, albumin-globulin ratio, and prothrombin time determinations. Abdominal exposure was obtained through an upper right rectus incision under ether anesthesia. Venous pressures were measured in a branch of the splenic or mesenteric veins and the portal vein was exposed. The common trunk supplying the middle and left lateral lobes was then ligated in each of the dogs and the branch to the right lateral lobe left intact. In five of the animals no attempt was made to occlude the hepatic artery. In six others the common hepatic artery or its left major branch was continuously occluded for varying periods of time, the longest interval being for one hour. In the remaining two animals the common hepatic artery was alternately clamped for 20 minutes and released for 5 minutes for total periods of time of 80 minutes and 120 minutes respectively. A wedge of liver was removed from the middle or left lateral lobe, equivalent in average weight to 9.1 per cent of the estimated weight of the liver. Some bleeding was encountered from the hepatic parenchyma: from branches of the hepatic veins immediately, and from those of the hepatic artery following removal of the arterial clamp. This bleeding was readily controlled in all instances by suture ligation of the individual bleeding points within the hepatic parenchyma.

When complete hemostasis had been obtained, the edges of the liver were approximated by interrupted sutures through the capsule on either side. Mattress sutures were not necessary in those animals in which the portal branch had been ligated but were necessary for hemostasis in the others. Portal pressures were again obtained and the abdomen closed with interrupted sutures.

Postoperatively the dogs were placed on oral fluids and on ordinary kennel rations as soon as they reacted from anesthesia. Antibiotics were not administered. Liver function studies were repeated periodically. After intervals of from two to six months the surviving dogs were re-operated upon under anesthesia. Portal pressures were measured and the animals then sacrificed and autopsied.

RESULTS

Ten of the thirteen dogs survived until they were electively sacrificed (Table I). Two died within twenty-four hours after operation. Death in the first

animal was due to technical error. The portal vein was injured during dissection, inadequately repaired, and death resulted from secondary hemorrhage. The second dog was poorly chosen for the procedure in that it presented evidence of poor liver function preoperatively as manifested by bromsulfalein retention of 63 per cent and reversal of the albumin-globulin ratio. It died twelve hours after ligation of the left main branch of the portal vein and continuous temporary occlusion of the common hepatic artery for forty-five minutes. Death was attributed to the prolonged hepatic anoxia in the presence of an already sick liver. This was the only animal to show histologic evidence of central liver necrosis.

TABLE I. OPERATIVE MORTALITY

EXTENT OF VASCULAR OCCLUSION	SURVIVALS	DEATHS
Ligation of left portal vein only	4	1
Ligation of left portal vein plus		
Continuous occlusion of left hepatic artery (15 min.)	1	0
Continuous occlusion of left hepatic artery (30 min.)	2	0
Continuous occlusion of common hepatic artery (45 min.)	1	1
Continuous occlusion of common hepatic artery (60 min.)	1	0
Ligation of left portal vein plus		
Intermittent occlusion of common hepatic artery (80 min.)	1*	0
Intermittent occlusion of common hepatic artery (120 min.)	1	0
Total	11	2

*Death of pneumonitis twenty-five days postoperatively.

The third dog died twenty-five days following ligation of the left main branch of the portal vein and intermittent occlusion of the hepatic artery for eighty minutes. Death was attributable to pneumonitis and distemper; liver function at the time of death was grossly normal.

All of the surviving animals exhibited some degree of lassitude and anorexia for approximately forty-eight hours postoperatively. Following this they became alert and rapidly regained their strength and appetite. All maintained their body weight without benefit of a special dietary regimen (Table II).

TABLE II. AVERAGE WEIGHTS, SACRIFICED DOGS

1. Preoperative weights of dogs	16.9 kg.
2. Postoperative (two months) weights of dogs	17.4 kg.
3. Estimated total liver weights	642 Gm.
4. Actual liver weights at autopsy	506 Gm.

Portal pressures following ligation of the major branch were elevated an average of 26 mm. H_2O above the preliminary pressures (Fig. 2). At the time of re-operation there was an average sustained increase of 22 mm. H_2O over the preoperative level. There were no significant differences in portal pressures in those animals whose hepatic arteries had been temporarily occluded. None of the dogs showed autopsy evidence of esophageal varices or gross enlargment of other collaterals.

One of the animals developed ascites. Its portal pressures varied significantly from the usual pattern and are not included in Fig. 2. It was found to have an initial portal pressure of 150 mm. H_2O, significantly above the nor-

mal. The pressure rose to 240 mm. H_2O at the time of operation and was sustained at 220 mm. H_2O two months later. Autopsy revealed a stricture of the major bile duct from the right lobe of the liver with consequent liver damage in addition to the typical changes incident to the ligation of the left portal vein branch. There was no evidence of hepatic vein thrombosis. These findings are consistent with those reported by Mann and co-workers[16] in dogs with previous ligation of the common bile duct.

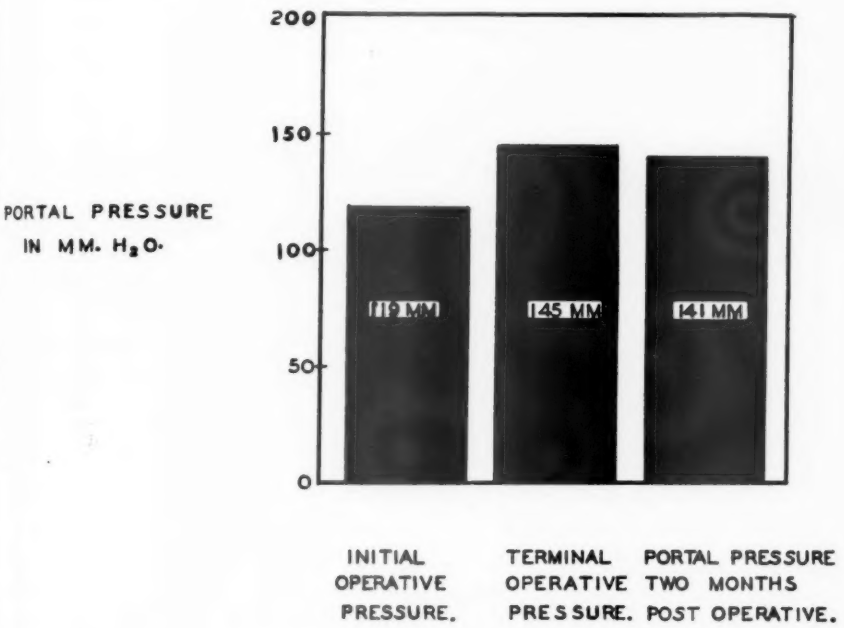

Fig. 2.—Average portal pressures.

Results of the liver function studies selected for use were not particularly informative. Blood bilirubin levels were not significantly altered. Bromsulfalein clearance likewise showed very little change. In only one instance was a retention of greater than 10 per cent found, either preoperatively or postoperatively. This dog, as previously mentioned, had a retention of 63 per cent preoperatively and died in the immediate postoperative period. The prothrombin levels were extremely variable and could not be interpreted as providing any significant information.

The changes in the serum protein levels were apparently the most significant of all the studies. In most of the dogs there was a slight decrease in the serum albumin levels postoperatively with consequent lowering of the albumin-globulin ratio. Only one of the dogs developed ascites or edema. The results obtained in liver function studies in a representative dog are presented in Table III.

At autopsy the ligature about the left portal vein branch was found to be intact in all dogs except one. The hepatic arteries were patent in all, even though temporarily occluded for long periods of time, and there was no instance of thrombosis of the hepatic veins. The central and left lateral lobes of the

B.

A.

Fig. 3.—Photomicrograph of hypertrophied right lateral lobe (*A*) and of atrophied left lateral lobe (*B*) of canine liver two months after permanent ligation of left portal branch and temporary occlusion of common hepatic artery. (Courtesy of the Department of Pathology, University of Michigan Medical School.)

liver were markedly atrophic in each case while the right lateral lobe was markedly hypertrophic. McMaster and Rous[20] found that the weight of the liver represents 3.45 per cent of the total body weight in the normal dog. On this basis, there was a reduction of total hepatic mass to only 78 per cent of normal (Table II) as a result of the partial hepatectomy and the vascular occlusion. There were no abnormalities of the gall bladder and no evidences of postoperative hemorrhage or of leakage of bile from the liver.

TABLE III. LIVER FUNCTION STUDIES

	SERUM BILIRUBIN (MG. PER CENT)	B. S. P. RETENTION (PER CENT)	SERUM PROTEINS		
			ALBUMIN GM. %	GLOBULIN GM. %	A/G RATIO
Preoperative	0.1	1.0	6.2	2.6	1.4
One week postoperative*	0.2	8.8	5.8	2.5	1.3
Two months postoperative*	0.1	8.2	6.0	2.9	1.1

*Results following ligation of left portal vein and continuous occlusion of common hepatic artery for 45 min.

Microscopic sections revealed atrophy and degenerative fatty infiltration of parenchymal hepatic cells in the segment deprived of portal blood (Fig. 3). In only one animal, previously discussed, was there evidence of central hepatic necrosis. There were no significant microscopic abnormalities of cells apparent in the remainder of the liver. Histologically the hypertrophied right lobe was indistinguishable from normal liver. The kidneys were examined and revealed no gross or microscopic abnormalities.

DISCUSSION

Whereas sudden ligation of the portal vein uniformly results in rapid death in the dog, in these studies it has been possible to carry out partial hepatectomy successfully by occluding all but that branch of the vein which supplies a relatively small segment of the liver. It had been initially feared that by interrupting portal blood flow through a large segment of the liver and simultaneously markedly increasing the blood flow through a small segment, hepatic function would be so greatly disturbed as to be incompatible with life. This has not proved to be true.

The consistent effect of sudden occlusion of the portal vein in the human being is not known. Cases have been reported[5] in which it became necessary during operation and the patients survived; others died. Child and co-workers[22] have demonstrated that the *Macaca mulatta* monkey survives portal ligation without ill effect. It is considered significant, however, that dogs which do not survive sudden complete occlusion of the portal vein have in most instances survived the marked interference in hepatic blood supply to which they have been subjected in these studies.

It has been demonstrated in this study that it is feasible to obtain a relatively bloodless approach to segments of the canine liver by permanently ligating major branches of the portal vein and simultaneously temporarily occluding the hepatic artery. This obviates the necessity of depending upon strangulating

mattress sutures through the hepatic parenchyma for postoperative hemostasis, which in itself was found to be poorly tolerated in control animals. In one of these dogs a relatively bloodless field was maintained for two hours by intermittent arterial occlusion. The common hepatic artery has been occluded as close to the celiac axis as possible in the later studies. This doubtless permits some arterial blood to reach the liver through collateral channels but only minimal gross arterial bleeding was noted from the incised surface. There are apparently no accessory portal veins in the dog.

The only significant physiologic changes consistently encountered in these animals have been a slight decrease in serum albumin and a slight increase in portal blood pressure. Neither of these have had an observable deleterious effect upon the dog. The development of ascites by one of the animals is disturbing but not discouraging inasmuch as the dog had an elevated portal pressure initially and was demonstrated at autopsy to have biliary obstruction of the only lobe of the liver which retained a complete blood supply.

The administration of antibiotics was deliberately omitted, although we were cognizant of the observations of Markowitz and co-workers.[8] It would doubtless have increased the margin of safety of the procedure but at the same time would have introduced another factor difficult to evaluate.

In patients with extensive lacerations of the hepatic parenchyma, bile peritonitis may develop as a result of the persistent leakage of bile from the parenchymal surface and prove to be a distressing or fatal complication.[2] It is of interest to note that there was no evidence of bile peritonitis in those animals which had deep wedge resections of liver parenchyma following ligation of the left branch of the portal vein.

These observations have not been subjected to clinical trial. One major deterrent is the technical difficulty of exposing the major branches of the portal vein in the human being. Satinsky[23] has, however, reported success in exposing this portion of the portal trunk during portacaval anastomosis by the ultilization of a right thoracoabdominal incision. Although the major branching occurs intrahepatically in some patients, Gilfillan[24] has found that the major branching does occur extrahepatically in approximately 85 per cent of cadavers.

If the technical difficulties can be surmounted, segmental occlusion of the portal blood flow would appear to be a rational and helpful adjunct to partial resections of the right lobe of the liver in human beings. Although indiscriminate permanent ligation of a major branch of the portal vein may not be routinely necessary or wise, it was accomplished in this relatively small number of dogs without prohibitive risk.

CONCLUSIONS

1. Permanent ligation of the branch of the portal vein supplying two of the three primary lobes of the liver and simultaneous temporary occlusion of the common hepatic artery are compatible with life in the dog and permit a relatively bloodless operative approach to the liver.

2. Such a procedure has not produced clinically significant physiologic disturbances in dogs studied as long as six months postoperatively.

3. Maintenance of uninterrupted portal blood flow through a relatively small segment of the liver materially reduces the risk of central occlusion of the remainder of the hepatic blood supply during partial hepatectomy in the dog.

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AUREOMYCIN IN EXPERIMENTAL ACUTE PANCREATITIS OF DOGS

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THE mortality from experimental acute hemorrhagic pancreatitis in the dog has been reduced by the use of penicillin.[1] This communication reports observations on the effect of aureomycin, administered by various routes, to dogs with acute hemorrhagic pancreatitis, together with data bearing on the etiology and pathology of the disorder.

METHOD

Hemorrhagic pancreatitis was produced in healthy mongrel dogs by a technique already described,[1] modified as follows: The accessory pancreatic duct, the largest of the two ducts in the dog,[2] was isolated at its entrance into the duodenum, in most instances without disturbing the blood supply to the duodenum. A sterile polyethylene tube, large enough to take a 19-gauge needle, was inserted through an opening into the duct and tied securely in place. After pancreatic juice for culture was obtained by aspiration of the duct; bile, aspirated from the gall bladder, or other fluid, was injected at a pressure of 450 to 600 mm. of mercury. Upon completion of the injection, the tube was removed and the duct was ligated on both sides of the opening. Immediately after the injection of bile, the pancreas was stained a mahogany color. The abdominal incision was then closed and the animal was offered food and water freely. Antibacterial therapy was given as indicated in Table I.

In addition to pancreatic juice, and bile, in many instances, pancreatic and liver tissue were taken for culture at the time of operation. Post-mortem cultures were taken from pancreas, bile, peritoneal fluid, blood from the portal vein and inferior vena cava, but only when they could be obtained immediately after death. To avoid surface contaminants, those from pancreas were obtained by injecting saline solution into the body of the pancreas and then aspirating it. In a few cases, heart's blood from dying dogs was taken for culture. Surviving animals were sacrificed on the twenty-first day.

All cultures were read after twenty-four hours, or, in the case of no growth, after forty-eight hours. After the organisms from the first few positive anaerobic cultures were specifically identified as *Clostridia welchii,* no effort was made in further instances to identify the specific species of Clostridia since the welch species predominates in the dog's intestine and abdominal viscera.[3, 4] The details of the antibiotic therapy given to certain groups of dogs are described under "Results."

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RESULTS

The results are summarized in Tables I and II.

TABLE I. RESULTS OF TREATMENT OF EXPERIMENTAL PANCREATITIS

GROUP	NUMBER OF DOGS	MATERIAL INJECTED INTO PANCREATIC DUCT	TREATMENT	SURVIVAL RATE (PER CENT)
1	2	15 c.c. saline solution	None	100
2	3	100 mg. aureomycin in 3 c.c. saline solution	None	100
3	2	100 mg. aureomycin in 15 c.c. saline solution	None	100
4	10	5 c.c. to 7½ c.c. bile	None	50
5	11	10 c.c. bile	None	9
6	2	100 mg. aureomycin in 10 c.c. bile	None	0
7	10	10 c.c. bile	Oral aureomycin preoperative	100
8	10	10 c.c. bile	Oral aureomycin postoperative	100
9	15	10 c.c. bile	Intravenous aureomycin postoperative	33
10	10	10 c.c. bile	Crysticillin IM 600,000 units postoperative	40
11	20	10 c.c. bile	Clostridia antitoxin preoperative	60

Groups 1, 2, 3.—Injection into the duct of 15 c.c. of saline solution, or of 100 mg. of aureomycin in 3 c.c. or 15 c.c. of saline solution, produced no evidence of subsequent illness. When the dogs were sacrificed and examined twenty-one days after injection, no pathology was found.

Group 4.—Two of five dogs injected with 5 c.c. of bile and three of five dogs injected with 7½ c.c. of bile, died within eighteen to seventy-two hours. At post-mortem they showed severe hemorrhagic pancreatitis, extensive fat necrosis of the omentum and peritoneum, and a small smount of bloody fluid in the peritoneal cavity. The surviving dogs, sacrificed after twenty-one days, showed no disorder apart from a shrunken, indurated, cordlike pancreas with scattered areas of fat necrosis.

Group 5.—Ten of eleven dogs injected with 10 c.c. of bile died within eighteen to seventy-two hours postoperatively. At post-mortem they showed severe hemorrhagic pancreatitis, widespread omental and peritoneal fat necrosis, and patches of fat necrosis on the pleural and pericardial surfaces. The surviving dog was very sick for about a week. At autopsy after sacrifice on the twenty-first day, a shrunken cordlike pancreas was found.

Group 6.—Two dogs received 100 mg. of aureomycin, dissolved in 10 c.c. of bile, injected into the duct. Both died quickly, fifteen and eighteen hours respectively, after operation, with necrosis of the entire pancreas and widespread fat necrosis. The changes in the pancreas were much more severe than those in dogs injected with bile alone. This was probably due to the destructive action of aureomycin upon tissue.

All dogs in the following groups were subjected to an injection of 10 c.c. of bile into the pancreatic duct, and received antibiotics as described below.

Group 7, Preoperative Aureomycin.—Each of ten dogs received 800 mg. of aureomycin in capsules in divided doses each day orally, until coliform

bacilli were absent in the feces for three successive days. This required from five to ten days. All of these dogs survived after an illness lasting for one to three days. Sacrifice when in apparent good health on the twenty-first post-operative day revealed a shrunken and indurated pancreas.

Group 8, Postoperative Aureomycin.—After twelve preliminary experiments in which the drug was administered immediately after operation it was found that many of the capsules had not dissolved, with a resulting mortality of 75 per cent. An additional ten dogs were given an initial 2 Gm. dose suspended in water by gavage immediately after operation. Thereafter, the same dose was given daily in capsules, for four days. All ten dogs survived after an illness lasting from one to three days. Sacrificed on the twenty-first day, when in apparent good health, they showed a shrunken, cordlike pancreas.

Group 9, Intravenous Aureomycin.—Ten dogs were treated by the intravenous injection of 300 mg. of aureomycin twice daily, with the first dose given immediately after operation. Seven of them died within eighteen to seventy-two hours, with the post-mortem findings described in Group 5. Three of five dogs treated with 400 mg. twice daily died in thirty to seventy-two hours. Survivors showed the same findings after twenty-one days as all other surviving dogs.

Group 10, Intramuscular Penicillin.—Ten dogs were treated postoperatively with 600,000 units of crystalline procaine penicillin G intramuscularly once daily, as suggested by Lewis and Wangensteen.[1] Six dogs died within fourteen to forty-eight hours—a mortality equal to that obtained by these observers. The four survivors were sick for two to four days.

BACTERIOLOGICAL DATA

The results of the bacteriologic studies are summarized in Table II. The data show that some three-fourths of all specimens of normal bile and pancreatic juice were sterile; whereas one-third or more of the biopsies of normal pancreas and liver contained bacteria. As others have also demonstrated,[4] Clostridia were the predominant organisms. The aerobes were rarely found and always in mixed culture.

TABLE II. BACTERIOLOGICAL FINDINGS IN NORMAL DOGS AND IN DOGS DEAD OF ACUTE PANCREATITIS

	NORMAL (PER CENT)				FATAL ACUTE PANCREATITIS (PER CENT)				
BACTERIA	BILE	PANCREATIC DUCT	LIVER	PANCREAS	BILE	PANCREAS	PERITONEAL FLUID	PORTAL VEIN BLOOD	VENA CAVAL BLOOD
Sterile	74	74	42	32	27	15	7	24	62
Clostridia	5	10	34	46	72	74	72	62	19
Coli	2	2	0.5	1	12.7	32	27	8	5.5
Pseudomonas	4	2.5	2	0.5	10.5	25		5.5	3
Streptococcus fecalis	1	0.5	2.5	3	14.8	21	21	5.5	5.5
Staphylococcus albus	0.5	0.5	0.5		6			3	
Staphylococcus aureus	3	4	4	4	4			8	
Diphtheroid	2	2.5	2.5	7.5	10.5			11	
Number of samples cultured	133	133	96	96	47	47	47	37	37

The incidence of Clostridia in pancreases of animals which succumbed to pancreatitis increased from 40 per cent to 74 per cent. Accompanying the increase was a substantial increase in the incidence of aerobes in mixed culture. The incidence of Clostridia in the pancreases of dogs which recovered from pancreatitis was 48 per cent, which is virtually the same as in the normal. However, the incidence presumably would have been higher in those which survived, as well as in those which died, had we cultured the pancreatic tissue directly, as was done in the case of the normal pancreas. The sharp rise in incidence of Clostridia in fatal hemorrhagic pancreatitis not only in pancreas, but in bile and pancreatic juice, is to be expected, since the organism as a saphrophyte should thrive in damaged or necrotic tissue. Consequently, we may not conclude from the frequency of its presence that this organism is necessarily involved in the lethal issue, particularly since it was still present in about one-half the pancreases of surviving animals following effective antibiotic therapy. The high incidence of Clostridia in the peritoneal exudate of fatal pancreatitis might be due to leakage from the pancreas. But the high incidence of Clostridia in portal vein blood as compared to blood in the inferior vena cava of animals dying of the disease excites the suspicion that the inflammation created in and by the pancreas facilitates the invasion of the portal system as well as the peritoneum by this and other species from the intestine.[5, 6]

Since examination of dogs several days after injecting the duct with bile and treatment with aureomycin discloses all the pathologic stigmata of hemorrhagic pancreatitis, the disease is not fatal if the superimposed infection can be controlled. That bacterial action is, in fact, the chief cause of death is clearly the case from a comparison of the survival rates of animals treated with aureomycin with those which were not. It appears that the bacteria causing death are primarily invaders from the gastrointestinal tract rather than those normally resident in the pancreas or liver, since aureomycin given orally is much more effective than that given parenterally.

The less effective action of the intravenous route has been repeatedly observed in experimental appendical peritonitis[7] and in experimental vascular injuries of the intestine.[8] This is due in part to the toxicity of the drug in dogs when given parenterally and in part to its weaker effect on intraintestinal flora.[7] Because the results with penicillin are no better than with intravenous aureomycin, the superiority of oral aureomycin cannot be ascribed to a better antibacterial effect on the Clostridia which have invaded the blood stream or are resident in the tissues, but to effective suppression of intraintestinal organisms, so that invasion of the blood and tissues from the intestine is either prevented or minimized.

The dominance of Clostridia led to further experiments (Group 11, Table I) intended to see whether Clostridia alone, or some other species, or the combined action of several species is responsible for the death in animals which do not receive effective antibiotic therapy. These experiments consisted of pretreatment of two groups of ten dogs with differing doses of Clostridial antitoxin* (½ ampule or 1 ampule per day for four days respectively). Sixty per cent of each group

*Lederle Gas Gangrene Antitoxin Polyvalent, Globulin-Modified.

recovered, a result superior to that obtained by the use of a parenteral antibiotic. It is hardly possible that passive immunity against Clostridia could be as effective as a parenteral antibiotic, if the Clostridia were not a dominant factor in the lethal process. A more rigid test of this conclusion might be achieved by an effort to obtain more complete protection against Clostridia by active immunization. This will be tried shortly.

It is, of course, hazardous to translate these observations to the corresponding condition in man. We have the impression from recent clinical experience at the Beth Israel Hospital that a higher rate of recovery from pancreatitis is being achieved in recent years. We know of no factor other than antibiotic therapy that can be properly credited with this turn of events.

SUMMARY

1. A lethal acute hemorrhagic pancreatitis was produced regularly in dogs by an injection of 10 c.c. of bile into the pancreatic duct.

2. Aureomycin given orally for several days before or after injection of the bile resulted in 100 per cent survival.

3. Intravenous aureomycin or parenteral penicillin therapy resulted in survival in only 40 per cent.

4. Bacteriologic studies confirm conclusions from earlier work that the normal liver and pancreas of dogs frequently harbor microorganisms, predominantly Clostridia.

5. In dogs dying of hemorrhagic pancreatitis there is a marked increase in bacteria, particularly Clostridia, in liver and pancreas as well as a high incidence of Clostridia in peritoneal fluid and in portal vein blood.

6. Since the survival rate by the prophylactic use of polyvalent gas gangrene antitoxin was 60 per cent, it is apparent that the Clostridia are a dominating influence in the lethal outcome of the untreated disease.

7. The much greater effectiveness of the oral as compared to the parenteral route of administration of the antibiotic indicates that the organisms which invade the tissues from the intestine following the onset of pancreatitis are the major source of the pathogenic organisms involved in the lethal outcome of this disease in dogs.

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CARCINOID TUMORS OF THE APPENDIX

A Review of Twenty-Six Cases

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THE carcinoid tumor or argentaffinoma is a unique and common neoplasm of the gastrointestinal tract. Carcinoid tumors occur from the stomach to the rectum and have been reported in ectopic bowel, such as Meckel's diverticulum.[1] However, they are far commoner in the small intestine and appendix. This report is a study of 26 cases of carcinoids of the appendix encountered in the Pathology Department of Touro Infirmary over a period of fifteen years.

The term carcinoid tumor has established itself through common usage. Oberndorfer[2] in 1907 used the name "carcinoid" for this tumor because of his belief that the neoplasm was benign, despite its resemblance to carcinoma. However, the medical literature for the next several years continued to confuse carcinoids with gland cell carcinomas of the appendix. Carcinoids were generally referred to as spheroidal-cell type of carcinoma. Gosset and Masson[3] noted the affinity of silver salts for the cells of carcinoid tumor and suggested that the neoplasm be called "argentaffin tumor." As case reports began to accumulate, it gradually became recognized that "carcinomas" of the appendix were two distinct histologic and clinical types: namely, carcinoids or argentaffinomas and gland cell adenocarcinomas similar to carcinomas found elsewhere in the gastrointestinal tract. It further became necessary to recognize a difference of clinical behavior as far as malignancy was concerned between carcinoids of the intestine and appendix. Most of the reports in the literature concerning the incidence of metastasis from carcinoids fail to make a distinction between appendical and intestinal carcinoids.

INCIDENCE

Carcinoids are the most frequent neoplasia of the appendix. Ackerman and Regato[4] noted that of the three types of appendical tumors, carcinoids represent 89 per cent, mucoceles 8 per cent, and adenocarcinomas 3 per cent. In 13,374 consecutive appendectomies at Touro Infirmary[5] from the years 1934 to 1948, there were twenty-six carcinoids. This is an incidence of 0.2 per cent of all appendectomies at our hospital. A review of the literature shows that in 187,580 appendectomies there were 283 carcinoids, an incidence of 0.15 per cent (Table I). Therefore, it can be expected that roughly one in every 500 appendectomies will reveal a carcinoid. It is important to emphasize that in a

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large percentage of cases the tumor is only recognized on microscopic examination of the appendix. Hence, the incidence of carcinoids will vary with the thoroughness of the microscopic study of the appendix. Longitudinal sections through the tip of the appendix for a distance of at least 1 cm. together with transverse sections of the middle and proximal thirds of the organ should demonstrate the smaller tumors. If longitudinal sections of the tip of the appendix are not done, many carcinoids will not be discovered.

TABLE I

AUTHOR	CARCINOIDS	APPENDECTOMIES	PER CENT CARCINOIDS
McWilliams[6]	26	6,505	.40
Mörl[7]	10	3,521	.29
Norment[8] (Mayo Clinic)	65	45,000	.14
Wyatt[9]	2	2,179	.09
Smith[10]	21	7,865	.27
St. George[11] (Bellevue Hospital)	7	9,108	.08
Moore[12]	10	10,299	.10
Porter and Whelan[13] (Boston City Hospital 1910-1937)	72	26,384	.28
Reitz[14]	2	2,520	.08
Hosoi[15]	3	195	1.54
Reimann[16]	14	13,151	.11
Pearson and Fitzgerald[17] (Boston City Hospital 1934-1948)	25	47,479	.06
Weiss[5] (Touro Infirmary 1934-1948)	26	13,374	.19
Total	283	187,580	.15

AGE AND SEX

The age incidence of carcinoids of the appendix will naturally be influenced by the age incidence of appendectomies. Forbus,[18] McKenty,[19] and Ackerman and Regato[4] all are agreed that the incidence is higher in the third decade of life. In our series, 52 per cent occurred between the ages of 20 and 30 years. Ackerman and Regato[4] reported the condition present in 80 per cent of cases in females; McKenty[19] reported 70 per cent in females. In our series 85 per cent occurred in females.

PATHOLOGY

The tip of the appendix is the common site of the lesion, producing a gross "drumstick" appearance. The cut surface has a yellow color and a rubbery consistency. The lumen of the distal end of the appendix is usually obliterated by fibrosis. Occasionally the growth is of multicentric origin and can only be recognized by sections through various levels of the appendix. The earliest tumors are seen in the submucosa of the appendix. Forty per cent of our series showed invasion of the muscular wall and serosa. There was no evidence of any lymph node metastasis or extension beyond the appendix in our series.

Masson[20] has given us an excellent description of the cells of carcinoids. He describes the typical cell as a small cell with an oval or round nucleus that has a well-defined nuclear membrane and a fine stippling chromatin. The cytoplasm is usually slightly acidophilic, granular, and often vacuolated. The cell membrane is indistinct and many cells appear to blend into a column with no

apparent delineation of their cytoplasm. They may form columns, nests, coils, or masses of cells. Occasionally rosettes or pseudorosettes are formed. The argentaffin properties of cytoplasmic granules have been mentioned. Others have ascribed chromaffin, plumbophilic, and muciphilic properties to the granules.[17] The argentaffin cells are found singly or in pairs among the columnar epithelial cells of the entire gastrointestinal tract. They are more numerous in the distal part of the ileum and the appendix. Whether the argentaffin cells represent an entodermal cell which arises in the intestinal epithelium or an ectodermal cell which has migrated to the intestinal epithelium from the chromaffin tissues of the body is still an unsettled question. Masson believed that carcinoids of the appendix resulted from autonomous proliferation of argentaffin cells associated with obliterated appendices containing neuromas. Porter and Whelan[13] suggested that carcinoids of the appendix are simply proliferating argentaffin cells associated with chronic inflammation and fibrosis of the appendix, while carcinoids of the intestine are true neoplasms. This would explain the difference in clinical course of the two types of carcinoids. In support of the high association of carcinoids of the appendix with fibrous obliterated appendices, 77 per cent of our twenty-six cases were associated with partial fibrous obliteration of the lumen of the appendix and 33 per cent of these cases showed microscopic neuromas within the fibrous tissue.

DIAGNOSIS

Preoperative diagnosis of carcinoid tumor of the appendix is not made either because there are no signs and symptoms of appendical disease or else the findings are those simulating appendicitis. In our series the preoperative diagnosis was appendicitis in twelve cases and in the remaining 14 cases the appendices were removed incidentally during a laparotomy. As the tumor is usually located at the tip of the organ, the vast majority of cases of carcinoids of the appendix are not associated with acute obstructive appendicitis. Only five of our twenty-six cases were associated with acute focal or suppurative appendicitis. A circumscribed yellow neoplasm found in the tip of an appendix is presumptive of a diagnosis of carcinoid. It is important to emphasize that there are no histologic criteria to recognize malignancy in carcinoids other than invasion beyond the appendix and metastasis.

PROGNOSIS AND TREATMENT

The vast majority of carcinoids of the appendix are clinically benign neoplasms. The prognosis of appendical carcinoids is excellent if the patient is treated by simple appendectomy, including the complete removal of the mesoappendix. The inability to separate histologically those carcinoids that will metastasize and those that will not has led many to consider all carcinoids malignant. Pearson and Fitzgerald[17] cited 38 per cent of their series of forty-two carcinoids of nonappendical site as showing regional lymph node or distant metastasis. However, none of their reported ninety-eight cases of appendical carcinoids showed evidence of metastasis. They collected twenty-three cases of metastasis from appendical carcinoids in the literature and thought that the

relative infrequency of metastasis from appendical carcinoids was due to the location of the tumor rather than to any essential difference between appendical and intestinal carcinoids. None of our twenty-six cases showed any evidence of spread beyond the appendix. There were no mortalities from the operative procedure.

SUMMARY

1. Carcinoid tumors are the most common neoplasm of the appendix. In 13,374 consecutive appendectomies at Touro Infirmary, twenty-six carcinoids were found, giving an incidence of 0.2 per cent. The reported incidence in the literature will depend greatly on the type of histologic examinations made on routine appendectomies.

2. Twenty of the twenty-six cases were associated with partial fibrous obliteration of the lumen of the appendix and arose at the tip of the organ. The preoperative diagnosis was appendicitis in twelve cases and in the remaining fourteen cases the appendix was removed during laparotomy. Only five cases were associated with histologic evidence of active inflammation. The location of the tumor at the tip does not usually predispose to obstructive appendicitis.

3. None of the twenty-six cases showed evidence of metastasis. Metastasis from appendical carcinoids as opposed to those of the intestines is extremely rare. There is a necessity to recognize a difference in clinical course between carcinoids of the appendix and intestine in spite of similar histologic findings.

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A LATERAL SUPRATENTORIAL APPROACH TO THE CEREBELLOPONTINE ANGLE FOR ACOUSTIC NERVE TUMOR

A Preliminary Report

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THE cerebellopontine angle, as usually approached surgically below the tentorium cerebelli, is the apex of a pyramid. The sides of the pyramid are: (1) superior: the undersurface of the tentorium; (2) medial: the pons, cerebellar peduncles, and lateral lobe of the cerebellum; (3) lateral: the posterior surface of the petrous pyramidal bone and the adjacent portion of the occipital bone. Hence, the deeper into the angle the surgeon proceeds, the more constricted is the field. To provide greater exposure, various surgeons have suggested incising the tentorium after elevating the occipital lobe, but all have attacked through the occipital bone just lateral to the mastoid process. This attack did enlarge the base of the pyramid of the surgical field but failed to alter the essential problem of a progressively narrowing exposure.

The present paper describes a temporal approach to the cerebellopontine angle. After retraction of the posterior part of the temporal lobe, the surgeon proceeds along the superior surface of the tentorium and reflects it where it overlies the angle. This maneuver opens the apex of the pyramid previously described and yields adequate exposure.

TECHNIQUE

The patient lies on his healthy side with the shoulders higher than the hips and the head in position for temporal craniotomy. The skull is entered through the posterior portion of the temporal squama because the tumor lies directly medial to the most posterior portion of the temporal muscle. The posterior portion of the inferior surface of the temporal lobe is retracted and reveals the middle fossa of the skull. If necessary for adequate retraction, the vein of Labbé is sacrificed. If there is excessive intracranial pressure, the ventricle may easily be tapped. Up to this point the procedure is similar to the intradural approach to the Gasserian ganglion.[3] However, in the present operation the cranial defect is larger and more posterior.

The petrous ridge and tumor lying beneath the tentorium are now palpated and the tentorial notch visualized. A single linear incision is made in the tentorium along the petrous ridge and carried forward to enter the notch (Fig. 1). This permits reflection of the triangular portion of the tentorium, which immediately overlies the tumor. The tumor seems to present itself for

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excision. However, it may be necessary to retract slightly posteriorly the uppermost part of the lateral lobe of the cerebellum. The tumor itself is dealt with as is customary, namely: intracapsular enucleation followed by as complete removal of the capsule as possible. The use of a dental or laryngeal mirror may assist in visualizing the portion of the tumor within the internal auditory meatus.[2] It is not necessary to repair the tentorial incision. Closure is without drainage.

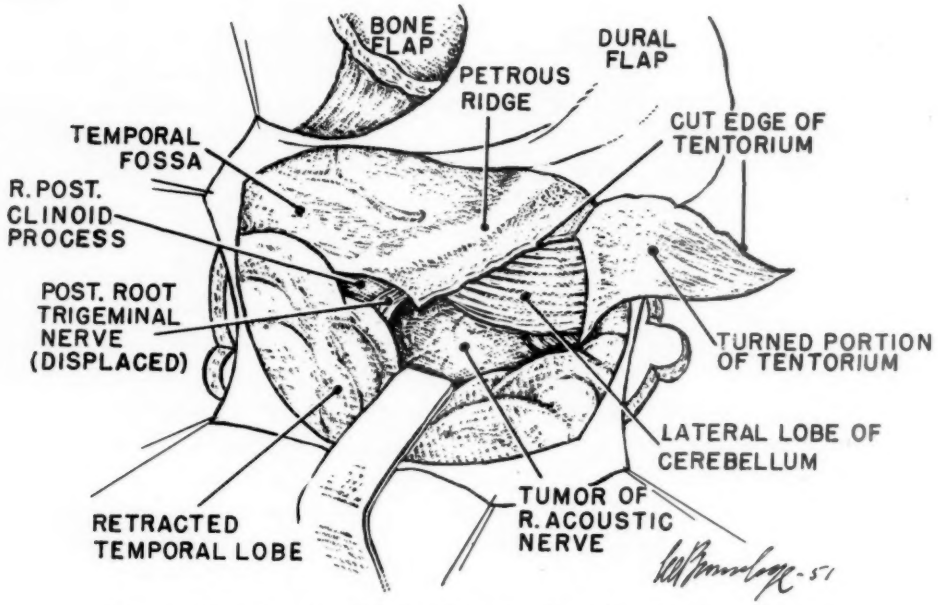

Fig. 1.—Drawing of surgical approach described (on right side).

DISCUSSION

Consideration of the tentorial and supratentorial relationship of acoustic neurinomas has led to the present technique, first carried out Oct. 26, 1950. Before the tumor itself is attacked, the tentorial notch is opened widely. This permits immediate restitution of flow of cerebrospinal fluid upward in the cisterna ambiens and downward in the aqueduct. Accordingly, this technique should be especially advantageous for those tumors with upward extension and those with transtentorial herniation of the brain stem.[1] It should likewise be especially useful for smaller tumors where the bulk of the tumor has not forced open an infratentorial surgical path by displacing cerebellum and brain stem. One sees the posterior root of the trigeminal nerve and its associated petrosal vein early. There is no retraction of the brain stem either directly or indirectly (through medial retraction of the cerebellum). This approach should prove worth while also for Gasseropetrosal tumors.

This approach has also been used to advantage: (1) in removing a meningioma extending both above and below the tentorium, (2) in exploring both surfaces of the tentorium, and (3) in cutting the tentorium along the ridge to relieve block of cerebrospinal fluid caused by massive intracranial extension of a tumor of the glomus jugularis.

A possible disadvantage is that the patient's position precludes simultaneous exploration of both pontocerebellar regions. But even in the rare and difficult case of bilateral acoustic nerve tumor, the opening of the tentorial notch may make it safe to wait some time before attacking the contralateral tumor. Another disadvantage is the possibility that retraction of the dominant hemisphere may occasionally cause transitory aphasia.

SUMMARY

A new approach to the cerebellopontine angle, especially for acoustic nerve tumors, is described. It consists of a posterior temporal craniotomy, retraction of the temporal lobe, and exposure of the superior surface of the tentorium. A linear tentorial incision along the petrous ridge forward to the incisura tentorii allows reflection of a triangular tentorial flap. This step promptly relieves obstruction to the flow of cerebrospinal fluid at the tentorial notch either downward through the aqueduct or upward through the ambient and pontine cisterns. At the same time the tumor presents itself with adequate exposure and without traction on the pons.

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MULTIPLE RIB FRACTURES; AN INDICATION FOR TRACHEOTOMY

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A FORMIDABLE group of pleural, pulmonary, cardiac, and cardiorespiratory complications are of frequent occurrence in patients sustaining multiple rib fractures. Appropriate treatment in severe injuries of this type is largely a matter of proper management of these various complications. Successful results require a degree of individualization of treatment which is seldom exceeded in any other injury. Inextricably part of the many facets of this problem is the requirement of keeping the tracheobronchial tree clear of blood and secretions. The recovery of the patient frequently depends largely on the proper management of this phase of treatment. To accomplish this objective, Novocain injections,[1-3] intratracheal catheter suction,[4] bronchoscopic aspirations,[4, 5] and operative treatment[6, 7] to immobilize the fractures have all been utilized with various degrees of success. A direct surgical approach to the problem by tracheotomy has not yet been reported.* It is the purpose of this article to record the experience gained in four patients on whom tracheotomy was done for this indication. In each instance immediate and outstanding benefits, which considerably exceeded expectation, were obtained. All of the patients recovered. Pulmonary complications did not develop in two patients operated upon early, and bilateral pneumonia present in two patients at the time the tracheotomy was done resolved after operation. The subsequent management of these patients was enormously facilitated when compared with that of others previously treated by alternative methods.

CASE 1 (Binghamton City Hospital, Service of Dr. J. J. Cunningham).—A 44-year-old man was injured June 12, 1950, in a head-on automobile accident. He sustained fractures of the right patella and the left tibia and fibula; in addition there were anterior fractures of ribs one to seven inclusive on the right side and one to four inclusive on the left side. On his admission to the hospital thirty minutes after the accident, it was found that the sternum and attached rib fragments were depressed and moderate paradoxical movement was present. The patient was pale but not cyanotic. A bedside roentgenogram demonstrated traumatic pneumonia of the left upper lobe (Fig. 1).

During the next twenty hours tracheobronchial secretions accumulated; cough was entirely ineffectual and produced violent paradoxical movement of the sternum and attached rib fragments. Several tracheal aspirations were necessary. The patient's chest was "wet," the respiratory rate was accelerated, moderately severe paradoxical movement was present, and cyanosis had developed. Twenty hours after the accident a tracheotomy was done and a No. 6

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*Since submission of this article, reference to tracheotomy has been found. Samson[17] has recommended the operation for patients having associated fractures of the jaw; Dickman and Baronofsky[18] have utilized the procedure in three patients having a "flail chest" injury and "wet lung."

Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—This anteroposterior supine bedside roentgenogram was exposed one hour after injury. The rib fractures are not seen in the reproduction. The infiltration in the left upper lobe is produced by a hematoma; the latter occurs more commonly in penetrating or perforating injuries.

Fig. 2.—This anteroposterior roentgenogram was exposed twelve days after injury. Resolution of the hematoma is almost complete.

Fig. 3.—The patchy atelectasis demonstrated in this roentgenogram developed during the first twenty-four hours following injury. Although the involvement was not extensive, temperature was 104° F. The exposure was made immediately before the first bronchoscopic aspiration.

size tube was introduced. Aspiration through the latter yielded about 15 c.c. of purulent secretion and immediately thereafter respiration was quiet; paradoxical movement decreased, and the patient's color was good without oxygen. Oxygen therapy was not required thereafter.

During the next forty-eight hours, tracheal suction was necessary at intervals of fifteen to thirty minutes, and each aspiration yielded about 5 c.c. of purulent bloodstained sputum. In addition to parenteral penicillin in doses of 50,000 units every three hours, 100,000 units dissolved in 2 c.c. saline solution was instilled into the tracheotomy tube at six-hour intervals. During this period, obvious symptoms of impending delirium tremens developed, and vigorous measures were taken to avoid this complication. Five days after injury, delirium tremens developed; restraint was necessary and two attendants were required most of the time. Extraordinary excitement occurred with each tracheal aspiration, which was accompanied by violent paradoxical movement of the anterior chest wall. Delirium tremens persisted for forty-eight hours; constant nursing attendance was required for ten days, at the end of which time tracheal secretions had become scanty and mucoid, and aspirations were required at intervals of only two or three hours.

During the second week, the chest wall became increasingly stable. A chest roentgenogram then demonstrated almost complete resolution of the hematoma in the left upper lobe (Fig. 2). The tracheotomy tube was removed twenty days after operation, at which time the chest wall was stable. The sinus filled in rapidly, and within another week the patient had made a complete recovery from the chest injury.

Comment.—In this patient, severe paradoxical movement of the sternum and attached anterior rib fragments occurred during cough, and for this reason the latter was entirely ineffectual. Consequently tracheobronchial secretions accumulated, causing bronchial obstruction and anoxemia, which in turn produced labored breathing, increasing the pain and paradoxical chest wall movement. This vicious circle was immediately broken by thorough tracheal suction after tracheotomy. During the immediate postoperative period a quantity of mucopurulent secretion, sufficient to drown the patient, was aspirated daily. The development of delirium tremens was managed without incident.

Case 2 (Ideal Hospital, Endicott, N. Y.).—A 61-year-old janitor fell down an elevator shaft Aug. 14, 1950, and sustained fractures of ribs four to eight inclusive on the left side. His condition was good when admitted to the hospital about one hour later. During the night, cough was ineffectual and tracheobronchial secretions began to accumulate. The following day, despite oxygen, the patient was dyspneic, cyanotic, and semiconscious, and temperature rose to 104° F. A chest roentgenogram demonstrated patchy atelectasis in both lungs (Fig. 3). A bronchoscopic aspiration was done in the patient's bed without anesthesia. Immediate improvement followed; the patient regained consciousness and his color was good without oxygen.

During the next forty-eight hours, despite frequent tracheal aspirations, his condition rapidly deteriorated. He became severely dyspneic and cyanotic; bubbling tracheal and bronchial râles were present; he perspired profusely; auricular fibrillation had developed, and cough and pharyngeal reflexes were entirely absent when tracheal aspirations were done. Another bronchoscopic aspiration was done, and a large amount of purulent tracheobronchial secretion was removed. Following the procedure, the tracheobronchial tree was dry but the patient remained in coma; dyspnea, cyanosis, and auricular fibrillation persisted. A chest roentgenogram (Fig. 4) demonstrated extensive bronchopneumonia in both lungs. He appeared moribund to all observers. Reflexes were absent, and a large urethral catheter was readily passed into the trachea. Oxygen was administered through this catheter, which was

also used at frequent intervals for aspiration. Purodigin and aureomycin were administered intravenously, ACTH and Adrenalin in oil were given intramuscularly, and this was followed by a transfusion of 500 c.c. of blood.

The patient's color improved when intratracheal oxygen was started, and during the night further improvement occurred. The following day a tracheotomy was done under Novocain anesthesia; oxygen was administered during the procedure through the intratracheal catheter. Postoperatively the patient was placed in an oxygen tent and oxygen was also administered through the tracheotomy tube. It was now possible for the first time to keep the tracheobronchial tree clear of secretions. Tracheal suction was required at ten- to fifteen-minute intervals, and each aspiration yielded about 5 c.c. of blood-stained purulent secretion. Penicillin in doses of 100,000 units, dissolved in 2 c.c. saline solution was administered through the tracheotomy tube at three-hour intervals.

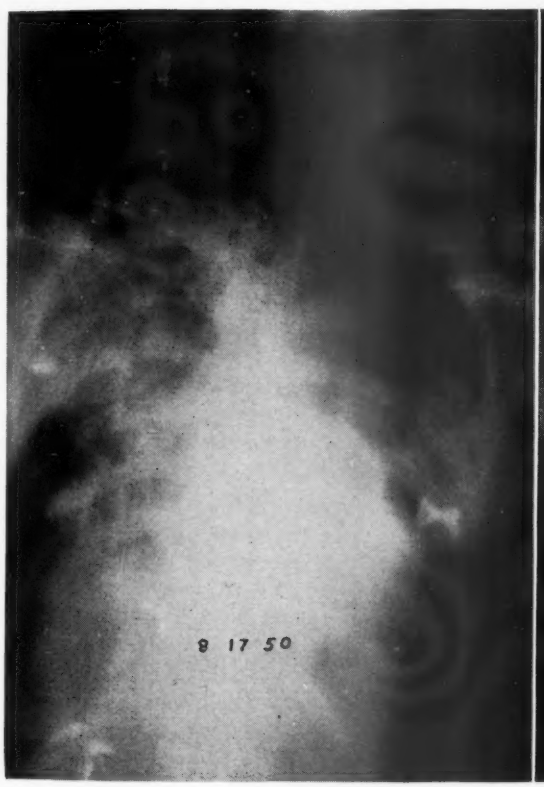

Fig. 4.

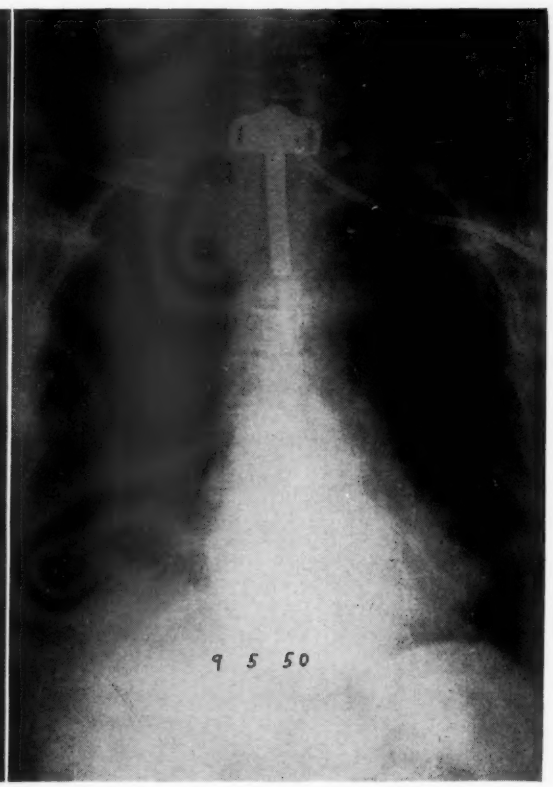

Fig. 5.

Fig. 4.—This roentgenogram was exposed three days after injury following a second thorough bronchoscopic aspiration. The patient was in coma and the film is blurred because of motion. The extent of the infiltration present is seldom seen except in postmortem studies.

Fig. 5.—This roentgenogram was exposed eighteen days after operation. The lungs were clear but the patient still required oxygen.

The patient improved rapidly following operation and a bedside roentgenogram taken on the third postoperative day demonstrated remarkable clearing of the pulmonary infiltration. Tracheobronchial secretions were then mucoid rather than purulent, and aspirations were necessary at intervals of about one to two hours. Subsequently the patient's pulmonary infiltration cleared rapidly, but the cardiac status remained unsatisfactory and signs of severe cerebral damage due to anoxia persisted. On September 5, nineteen days after injury, the lungs were clear and the fractures were healed (Fig. 5). At this point it seemed certain that severe cerebral damage would be permanent. To our surprise he then began to improve. On October 11 the tracheotomy tube was removed; the patient was discharged on Oct. 21, 1950.

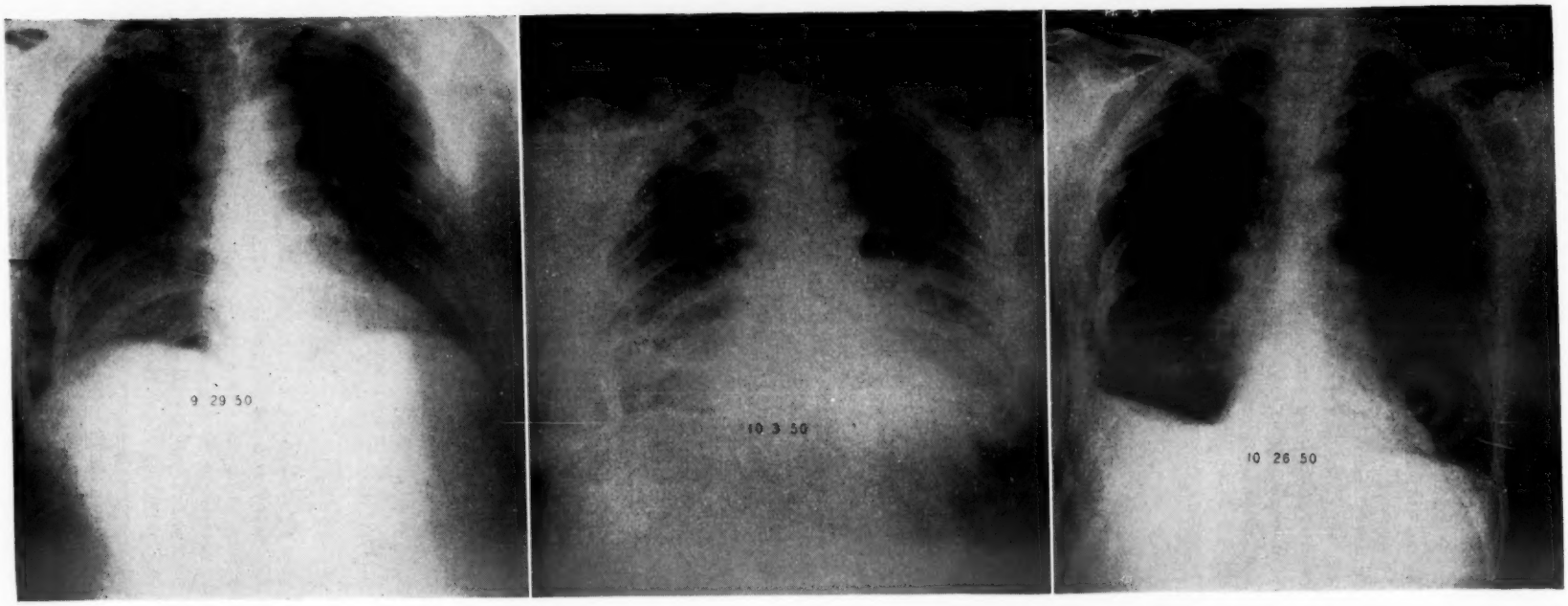

Fig. 6. Fig. 7. Fig. 8.

Fig. 6.—This roentgenogram was exposed about two hours after injury. The posterior fragments of the seventh and eighth ribs are driven inward and a small pneumothorax is present.

Fig. 7.—This roentgenogram was exposed about twelve hours after thoracotomy and tracheotomy. A drainage tube is still in position; the patient was receiving oxygen through the tracheotomy tube. The right lung is fully expanded. The bilateral pneumonia present before operation is demonstrated.

Fig. 8.—This roentgenogram was exposed a few days before the patient was discharged from the hospital. It demonstrates obliterative pleurisy and is not otherwise remarkable. Some depression of the remaining posterior fragments of the fractured seventh and eighth ribs is present.

Some indications of cerebral damage are still present at this writing. Experience with this patient serves to re-emphasize the surgical rule that when tracheotomy is required the operation should be done early.

Comment.—There appears to be no doubt that tracheotomy was a life-saving measure in this patient. With intensive treatment his extensive bronchopneumonia cleared rapidly and the combination of frequent efficient tracheobronchial aspirations and intratracheal administration of oxygen permitted sufficient exchange to sustain life during this critical period. The persistent mental changes due to cerebral anoxia could doubtless have been prevented if the operation had been done sooner.

CASE 3 (Maimonides Hospital, Liberty, N. Y.).—A 42-year-old construction worker was run over by a bulldozer Sept. 29, 1950, while working on a fill operation. The machine threw him forward on his face on freshly dumped soil and then passed over him twice. On admission to the hospital about one hour later he was in mild shock, his color was fairly good, and no severe respiratory distress was present. A chest roentgenogram demonstrated fractures of ribs six to eleven inclusive on the right side, and a fracture of the right scapula. The posterior fragments of the seventh and eighth ribs were driven inward and a small pneumothorax was present; otherwise the lungs were clear (Fig. 6).

Tracheobronchial secretions began to accumulate immediately and cough was almost entirely ineffectual. Temperature mounted steadily and reached a peak of 104.2° F. within forty-eight hours, and at the same time the pulse rate rose to 130. The patient became increasingly dyspneic and cyanotic despite oxygen. He perspired profusely and at times was confused and disoriented. Sixty hours after admission a second roentgenogram demonstrated pneumonia in both lower lobes. At this time the patient was transferred to Binghamton City Hospital by ambulance. An operation was done about two hours after admission. An intratracheal catheter was introduced under local anesthesia. This excited a severe coughing paroxysm and about 15 c.c. of heavy green purulent material was aspirated. Under local anesthesia an incision about six inches long was made in the mid-axillary area at the site of the seventh and eighth ribs, which were driven into the pleural space. When the fractures were exposed, a large rent in the pleura was found; the sucking wound was closed with a moist laparotomy pack and general anesthesia with cyclopropane* was induced. Wiring of the rib fragments had been planned, but because of the patient's poor condition, resection of three and one-half inch segments of the two in-driven posterior rib fragments was done. Drainage of the pleural space with a large catheter was provided and this was connected to a conventioned water-seal deflation system. The wound was closed with 000 and 0000 cotton sutures.

With the patient under local anesthesia a tracheotomy was done and a No. 6 size tube was introduced. The patient was returned to the ward, oxygen was administered through the tracheotomy tube, and aspirations, which yielded about 5 c.c. of purulent bloodstained secretions, were done at intervals of ten to fifteen minutes during the immediate postoperative period. Penicillin was administered intratracheally and intramuscularly, and in addition streptomycin, 0.5 Gm. twice daily, was started. Immediate improvement followed operation. The following morning the patient's temperature was 101° F., pulse was 100; the right lung was fully expanded (Fig. 7).

Recovery was without incident, although two weeks were required for resolution of the pneumonia in the left lung. Solid union of the fractured ribs permitted the tracheotomy tube to be removed twenty days after operation. A chest roentgenogram taken three days before his discharge from the hospital is shown in Fig. 8.

Comment.—Although this patient's injury was unusually severe, the condition immediately following the accident was surprisingly good. Bilateral

*Administered by Dr. L. Payes.

pneumonia developed within sixty hours due to the accumulation of tracheobronchial secretions and ineffectual cough. The in-driven rib fragments presented an indication for operation. Exposure of the fractures revealed a large rent in the pleura. The sucking wound thus produced necessitated the induction of general anesthesia which was poorly tolerated by the already anoxic patient. This experience shows that operative fixation of rib fragments should not be undertaken lightly and that when such a procedure is done the operator should be prepared to cope with an open pneumothorax.

Although this patient's rib fractures were not immobilized, improvement followed immediately after tracheotomy, and thorough clearing of the tracheobronchial tree by suction. Experience with this patient supports the writer's view that the indirect benefits of operative fixation of rib fragments (relief of pain and stabilization of the chest wall which permits effectual cough) can be gained more safely, more easily, and more dependably by tracheotomy.

CASE 4 (Binghamton City Hospital).—On March 8, 1951, an obese 59-year-old construction worker fell fifteen feet from a roof to a fire escape and then rolled down a flight of stairs. On admission to the hospital a short time later his general condition was excellent. Roentgenograms of the chest demonstrated fractures of ribs five to eleven inclusive on the left (three of these were double fractures), and ribs five to eight inclusive on the right side. During the next twelve hours the patient became a little dusky and oxygen therapy was started. The patient was a heavy smoker and admitted having a "cigarette cough." Within forty-eight hours tracheobronchial secretions began to accumulate; his cough was ineffectual because of excruciating pain, and several attempts to perform tracheobronchial suction with a catheter were made. This procedure precipitated severe coughing paroxysms, vomiting, laryngeal spasm, and alarming cyanosis. Seventy-two hours after injury, coarse bronchial râles were present in both lungs; the patient was dusky, moderately dyspneic, and the pulse rate was 130. A tracheotomy was done under local anesthesia and a No. 6 tube was introduced. Tubation produced a severe coughing paroxysm and about 30 c.c. of heavy purulent secretion was expelled.

The patient was considerably improved immediately following operation. Intratracheal oxygen was required continuously for a period of twelve hours. Penicillin was administered intratracheally and parenterally as previously described. After twelve hours continuous oxygen was not required, but for a period of two or three days it was administered for a few minutes after each tracheal aspiration.

Twenty-four hours after operation the patient's abdomen became greatly distended, and a roentgenogram demonstrated acute dilatation of the stomach. Wangensteen suction was required for a period of forty-eight hours. Except for this complication, recovery was without incident. The patient was sitting up in bed twenty hours after operation and was ambulatory on the fourth postoperative day.

Twelve days after operation (fifteen days after the accident) there was very little instability of the chest wall, and cough was painless and effectual. The tracheotomy tube was removed at this time. The sinus filled in rapidly and was closed within two days. The patient was discharged from the hospital in excellent condition March 27, 1951, twenty days after the accident.

Comment.—In this patient severe pain and paradoxical movement of the chest wall prevented effectual cough. Tracheobronchial secretions accumulated during a three-day period, producing severe anoxia. Tracheotomy was followed by immediate relief and, except for the complication of acute dilatation of the stomach, recovery was without incident. The tracheotomy tube

was removed before the rib fractures were solidly healed but at this time cough was effectual and painless. The operation was done early, before pulmonary complications had developed.

DISCUSSION

The average case of a patient having multiple rib fractures in whom pulmonary complications develop due to the accumulation of tracheobronchial secretions follows a rather definite pattern. On admission to the hospital the patient's condition is usually fairly good. Within twenty-four to forty-eight hours tracheobronchial secretions accumulate in sufficient quantity to require oxygen therapy and the improvement that follows this treatment effectively masks the impending atelectasis and pneumonia. Twelve to twenty-four hours later one of the above complications has developed, and the patient is then dyspneic and cyanotic, despite oxygen. Active treatment is commonly delayed until this point is reached. This course occurs more frequently in men than in women, apparently because the heavy smokers among the former commonly develop a purulent tracheobronchitis with copious secretion within the first two or three days after injury. If the patient is in an older age group and has pulmonary emphysema and impaired pulmonary function, the difficulties in management are substantially increased.

The factors which impair the cough in these patients do not differ greatly from those operating in patients having thoracic wounds.[5] In order of their importance they are: (1) pain and fear of pain caused by coughing; (2) dyspnea due to pleural or pulmonary complications; (3) paradoxical movement of chest wall; (4) morphine narcosis; (5) cerebral anoxia; and (6) shock.

From a practical point of view it is convenient to consider these patients in two categories: those who are "unwilling" to cough, and those who are "unable" to cough. In the first group, pain and fear of the pain caused by coughing is the responsible factor and this should not ordinarily pose a difficult problem in treatment. In these patients effectual cough can almost always be established by the application of elastic bandages, the judicious administration of narcotics, and perhaps intercostal nerve block, provided proper assistance and encouragement are given.

Among those who are "unable" to cough tracheal suction or bronchoscopic aspiration will be required. The latter group can be further divided into two additional categories: those whose tracheobronchial tree can be kept clear by infrequent aspirations by these methods or who, after a few such treatments, are then able to cough effectually, and those who require frequent aspirations by tracheal catheter or bronchoscopy, and in whom effectual cough is not thereby established. The latter are the patients for whom tracheotomy is proposed. The operation should be done as soon as it is seen that the tracheobronchial tree cannot be kept clear of secretions by alternative methods. Ordinarily it should be possible to make this decision within twenty-four to forty-eight hours after injury and before pulmonary complications have developed.

Until comparatively recently, the indications for tracheotomy have been largely limited to patients having inflammatory or neoplastic obstructive lesions of the larynx. During the recent war the operation was commonly done for the purpose of aspirating the tracheobronchial tree in patients having severe maxillofacial injuries.[8, 9] Impressive results with this operation have recently been reported in patients having bulbar poliomyelitis,[10] tetanus,[11, 12] and severe head injuries.[13] Bailey and Monsour[14] reported the recovery of a patient who was in desperate condition following a postpneumonectomy thoracoplasty, and he has also found the operation useful postoperatively in other thoracic patients.[15] In a recent careful study, Reynolds and his associates[16] considered the indications for tracheotomy following resection of the esophagus. Among eleven patients, a tracheotomy was done in six, with one death. There were four deaths and one recovery among the remaining patients on whom a tracheotomy was not done. Three of the six tracheotomy operations were done prophylactically.

From the foregoing, it is seen that there is now considerable precedence for the use of tracheotomy in patients requiring frequent dependable tracheobronchial aspiration. It follows logically that it should be equally useful, if not actually more beneficial, in the group of patients under discussion having multiple rib fractures. Tracheotomy provides an absolutely dependable method of clearing the tracheobronchial tree at any hour and at an instant's notice. After operation the average nurse is an entirely adequate attendant. The alternative of treating these patients by repeated tracheal suction and bronchoscopy, besides being less efficient and more exhausting to the patient, requires extraordinary skill and places unusual demands on the time of the resident staff. As a matter of fact, the availability of the resident staff and the proficiency of the residents in these techniques are most important considerations in weighing the indications for tracheotomy. The operation, in addition to insuring a clear tracheobronchial tree, permits the intratracheal administration of penicillin, which is probably by far the most effectual method of administering this antibiotic to these patients. It also allows oxygen to be delivered intratracheally in concentrations approximating 100 per cent, a matter of no little importance in anoxic patients with widespread bronchopneumonia, as seen in Case 2. Experience with this patient suggests that the operation actually might have an application in certain patients having nontraumatic pneumonia if excessive tracheobronchial secretions, ineffectual cough, and anoxia are prominent features, and the patient has not had the benefit of antibiotic therapy.

SUMMARY

The problem of keeping the tracheobronchial tree clear of blood and secretions in patients having multiple rib fractures is discussed. These patients are considered in two groups: those who are "unwilling" to cough and those who are "unable" to cough. Tracheotomy is recommended for those patients in the second category if frequent tracheal or bronchoscopic aspirations are required. Suction through the tracheotomy tube insures a

clear tracheobronchial tree at all times and effectually protects the patient against lethal pulmonary complications. The operation also provides the important additional benefits that follow the intratracheal administration of oxygen and penicillin.

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MIXED TUMORS OF THE SKIN: CRITERIA FOR DIAGNOSIS

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ONE of the commonest surgical procedures is the removal of small isolated cutaneous neoplasms either for cosmetic reasons or to rule out the possibility of malignancy. Consistent and consecutive micropathologic studies would reveal that many of these small growths are not the usual neurofibromas, hemangiomas, nevi, or sebaceous cysts, but fall into the category of the uncommon. Into one such category can be placed tumors which contain an admixture of ectodermal and mesodermal elements. It is, therefore, our purpose to define more clearly these unique neoplasms, to differentiate them from similar growths, and to present two additional cases to the limited number thus far reported in the literature.

CRITERIA FOR DIAGNOSIS

Although the origin of these new growths is still a controversial subject, this group of benign neoplasms is a definite clinical and histologic entity formed by an aggregate of tissues which can be considered as owing their derivation to the ectoderm and mesoderm.[17]

To define these tumors more clearly, we have arbitrarily set up three criteria which we consider helpful in the diagnosis:

1. The neoplasm must be located in the skin except in that area which developmentally may contain misplaced remnants of salivary gland tissue. This would, therefore, include the parotid region, submaxillary region, cheek, lips, mouth, and the suprahyoid area of the neck. These areas theoretically disqualify these tumors because they may contain aberrant salivary gland tissue. It may be recalled that salivary tissue is developed from invaginated shelf-like projections of the mandibular and maxillary portions of the first branchial arch, which is the embryonal anlage of the parotid, submaxillary, and sublingual glands.[16]

2. The neoplasm should have tissues which resemble cells derived from the ectodermal and mesodermal germ layers.

3. Although the very common mixed tumor of the parotid gland rarely metastasizes, to exclude the possibility of this tumor giving rise to mixed tumors in the skin there should be no evidence of that neoplasm in the salivary glands.

Although most cutaneous neoplasms will be, as previously mentioned, neurofibromas, hemangiomas, nevi, and lipomas, one should also consider sebaceous gland adenoma, spiradenoma, adenocystic epithelioma of Brooke, dermoid cyst, and basal-cell carcinoma in the differential diagnosis. Some authors believe that mixed tumors are in reality a form of basal-cell carcinoma.[1] The diagnosis of mixed tumors of the skin will rest primarily on the microscopic section;

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neither the gross appearance nor the location will aid in differentiation. The locations thus far recorded in the literature (Fig. 1) favor no particular area of the body, although in thirty-four out of thirty-six cases in which an area was mentioned, the most common sites were the scalp (8), the hand (5), the finger (4), and the nose (4).

RÉSUMÉ OF TYPICAL CLINICOPATHOLOGIC PICTURE

A careful review of the literature revealed that there were thirty-four instances of true mixed tumors of the skin, to which we have added two of our own, thus making a total of thirty-six cases. Reference to Table I will give a brief summary of the pertinent data.

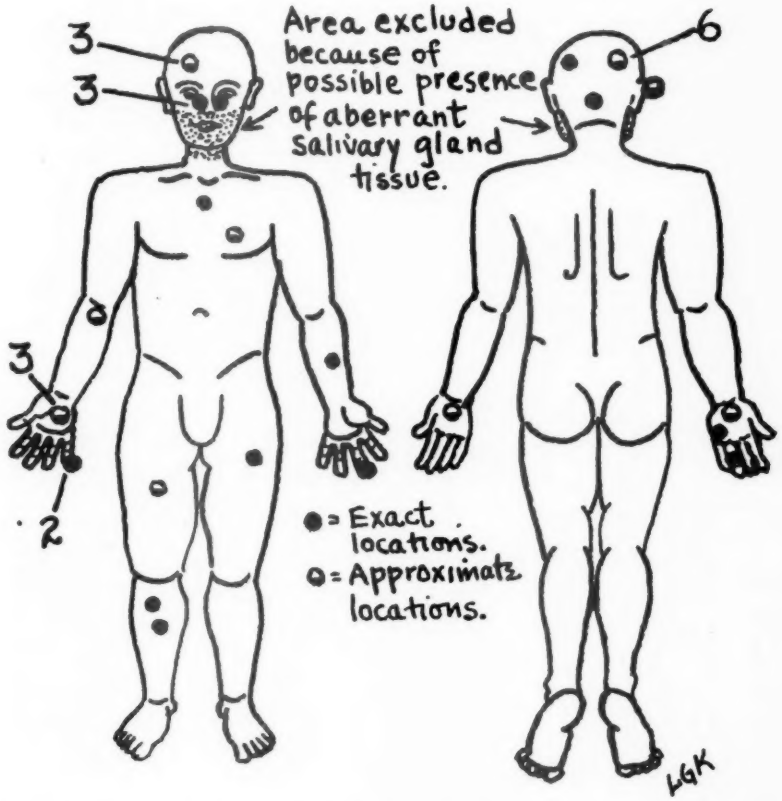


Fig. 1.—Mixed tumors of the skin. The illustration shows the location of thirty-four out of thirty-six cases recorded in the literature, including the two cases in this report.

A profile of the clinical picture reveals no clear-cut characteristic of diagnostic value. The sex incidence was nonspecific, there being fourteen males, nine females, and thirteen unrecorded. The duration of these tumors may be from three months to forty years; in nineteen instances in which the duration was specifically stated, the average was six and one-half years. This indicated that these growths are undoubtedly of a benign nature, thus differing from the more common parotid gland tumor; also no evidence of recurrence was noted following removal of any of these tumors. In only two out of twenty-eight in-

TABLE I. SUMMARY OF THIRTY-SIX CASES OF MIXED TUMOR OF THE SKIN

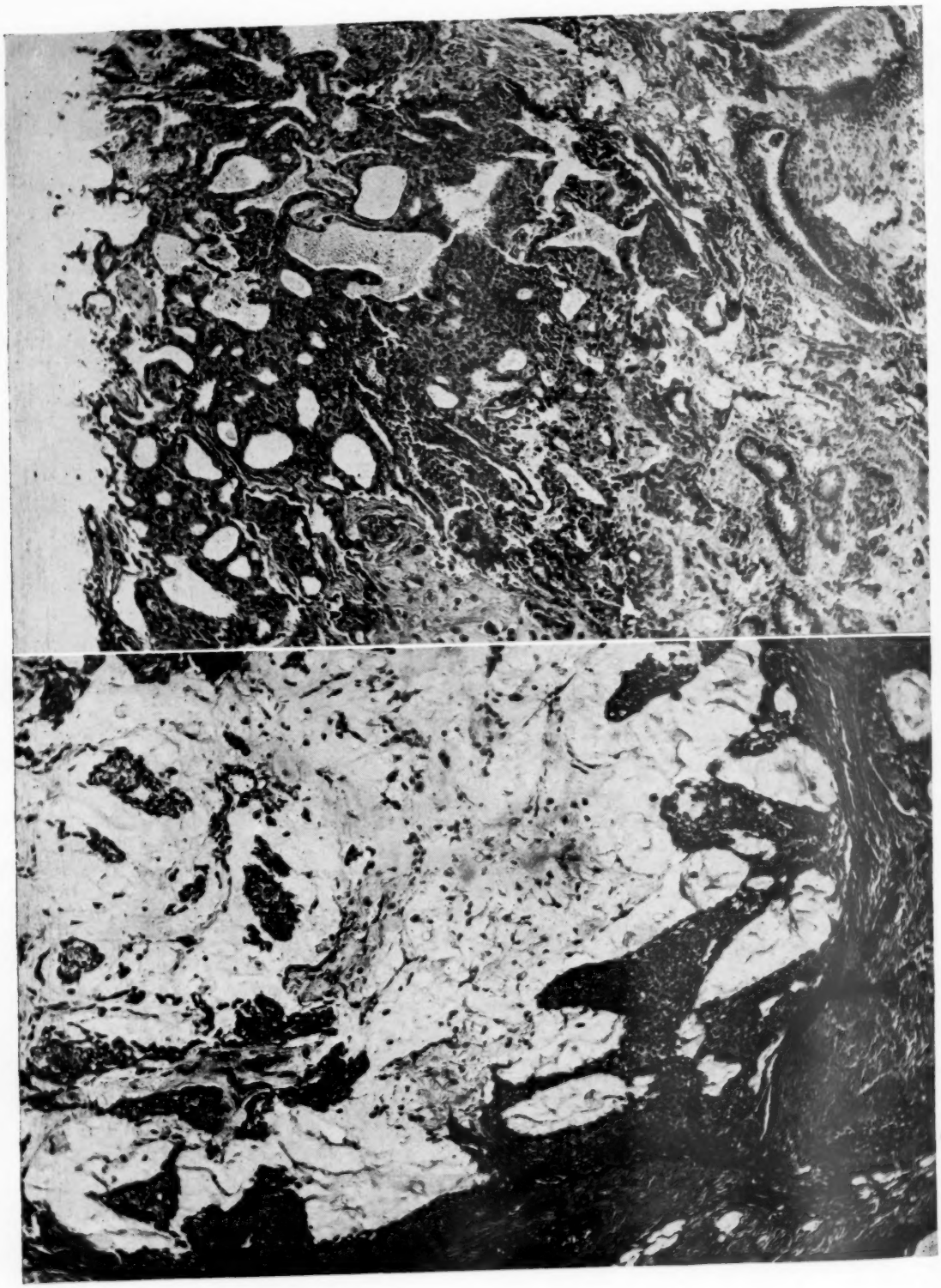
CASE	AUTHOR	YEAR	AGE	SEX	SITE	DURATION	TRAUMA	TISSUES REPORTED ON MICROSCOPIC SECTION
1	Tessmann	1911	40	F	Wrist, dorsum	4 yr.	0	Cartilage, lymphoid, mucoid, fibrous
2	Moulonguet and Peynet	1927	25	F	Forehead	3 mo.	0	Pseudo-glands, racemose glands, fibrous, myxomatous
3	Moulonguet and Peynet	1927		M	Forehead	3 mo.	0	Epithelium, fibrous, vascular (mitoses)
4	Erb	1930	59	M	Scalp, left parietal region		+	Epithelium, cartilage, "mammary" epithelium
5	Brunschwig	1931	26	M	Forehead		0	Epithelium, amorphous, giant cells, myxomatous
6	Kreibig	1931	38	M	Leg, right	6 yr.	+	Epithelium (pearl formation), cartilage
7	Kreibig	1931	30	M	Forearm, left	3 yr.	0	Epithelium, fibrous, homogenous "ground" substance
8	Hirsch	1933	34	F	Thigh, left		0	Epithelium, cartilage (mucoid degeneration and necrosis)
9	Halpert	1933	60	M	Nose, inner canthus	1 yr.	0	Epithelium, fibrous tissue, cartilage, bone, and bone marrow
10	Gaehtgens	1935	66	F	Finger, right, digit IV	2 yr.	0	Epithelium, mucoid, cartilage
11	Vidari	1935	48	M	Leg	40 yr.	0	Epithelium, mucoid, cartilage, fibrous
12	Geschickter and Koehler	1935			Scalp		0	All three showed basal epithelial cells, amorphous material, hyaline, and mucoid tissue
13	Geschickter and Koehler	1935			Elbow, flexor surface		0	
14	Geschickter and Koehler	1935			Hand, dorsum		0	
15	Scharla	1936	30	F	Hand, right, digit V		0	Epithelium, myxomatous, fibrous
16	Cade*	1937						
17	Cade	1937						
18	Simard	1938	76	F	Hand	10 yr.		Epithelium, nevi-form cells, sweat glands, mucoid, fibrous, cartilage

TABLE I—CONT'D

19	Uggeri	1939	29	M	Hand, left, digit III	1½ yr.	0	Epithelium, myxomatous, cartilage
20	Cid	1939			Hand		0	
21	Hollander	1940	40	M	Hand, digit V	3 yr.	0	Epithelium, hyaline, amorphous tissue
22	Gates, Warren, and Warvi†	1943			Hand			In all of these tumors, mucoid, hyaline, and fibrous tissues were present as well as one or all of osteoid, bone, and cartilage; in three tumors hair follicles were involved
23	Gates, Warren, and Warvi†	1943			Scalp			
24	Gates, Warren, and Warvi†	1943			Scalp			
25	Gates, Warren, and Warvi†	1943			Scalp			
26	Gates, Warren, and Warvi†	1943			Scalp			
27	Robbin	1943			Scalp		0	Epithelium, mucoid, cartilage
28	Robbin	1943			Leg		0	Epithelium, mucoid, cartilage
29	Highman	1944	80	M	Hand, left	5 yr.	0	Epithelium, myxomatous, cartilage
30	Morehead	1945	64	F	Breast	10 yr.	0	Epithelium, fibrous, atrophic sweat glands, fibrocartilage
31	Morehead	1945	69	M	Nose	10 yr.	0	Epithelium, myxomatous, lymphoid, chondromatous
32	Morehead	1945	38	F	Chest: sternal area of skin	2 yr.	0	Fibrous, sweat and sebaceous glands, myxomatous
33	Morehead	1945	53	F	Ear, superior surface	10 yr.	0	Epithelium, myxomatous, collagenous
34	Rabinovitch	1948	36	M	Nose, bridge	2 yr.	0	Epithelium, fibrillar cartilage, mucoid
35	Khedroo and Casella	1951	27	M	Nose, left side	2½ yr.	0	Epithelium, mucoid, bone, cartilage
36	Khedroo and Casella	1951	37	M	Scalp, mid-occipital	12 yr.	0	Epithelium, myxomatous, epithelial pearls, peri-endothelial hyperplasia

*Cade reported on 254 mixed tumors of which two occurred in the skin; however, no further data on these two neoplasms were given.

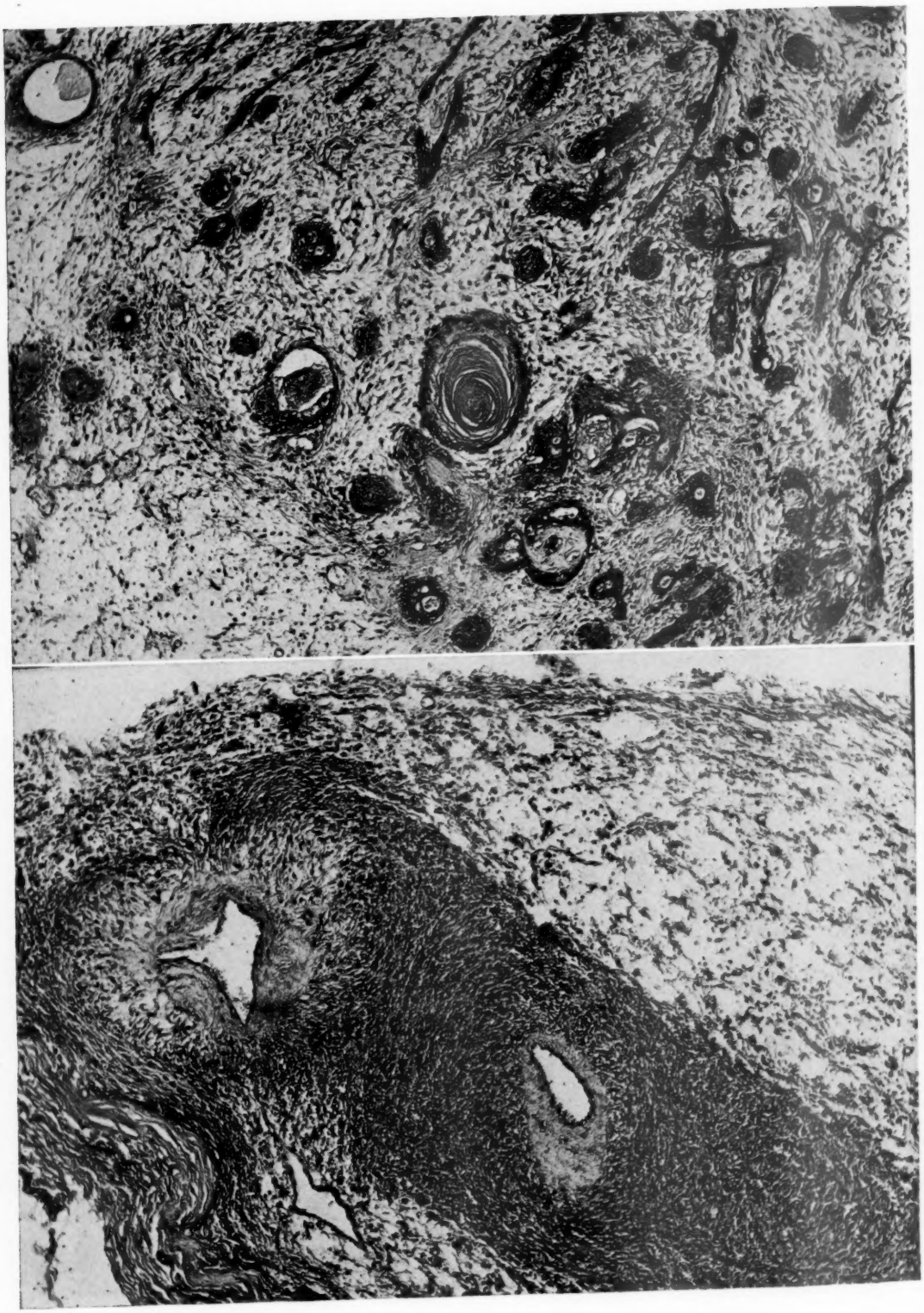
†Five mixed tumors of skin reported as part of a group which resembles sweat gland neoplasms. An extensive discussion of sweat gland tumors makes up the major portion of this monograph.



B.

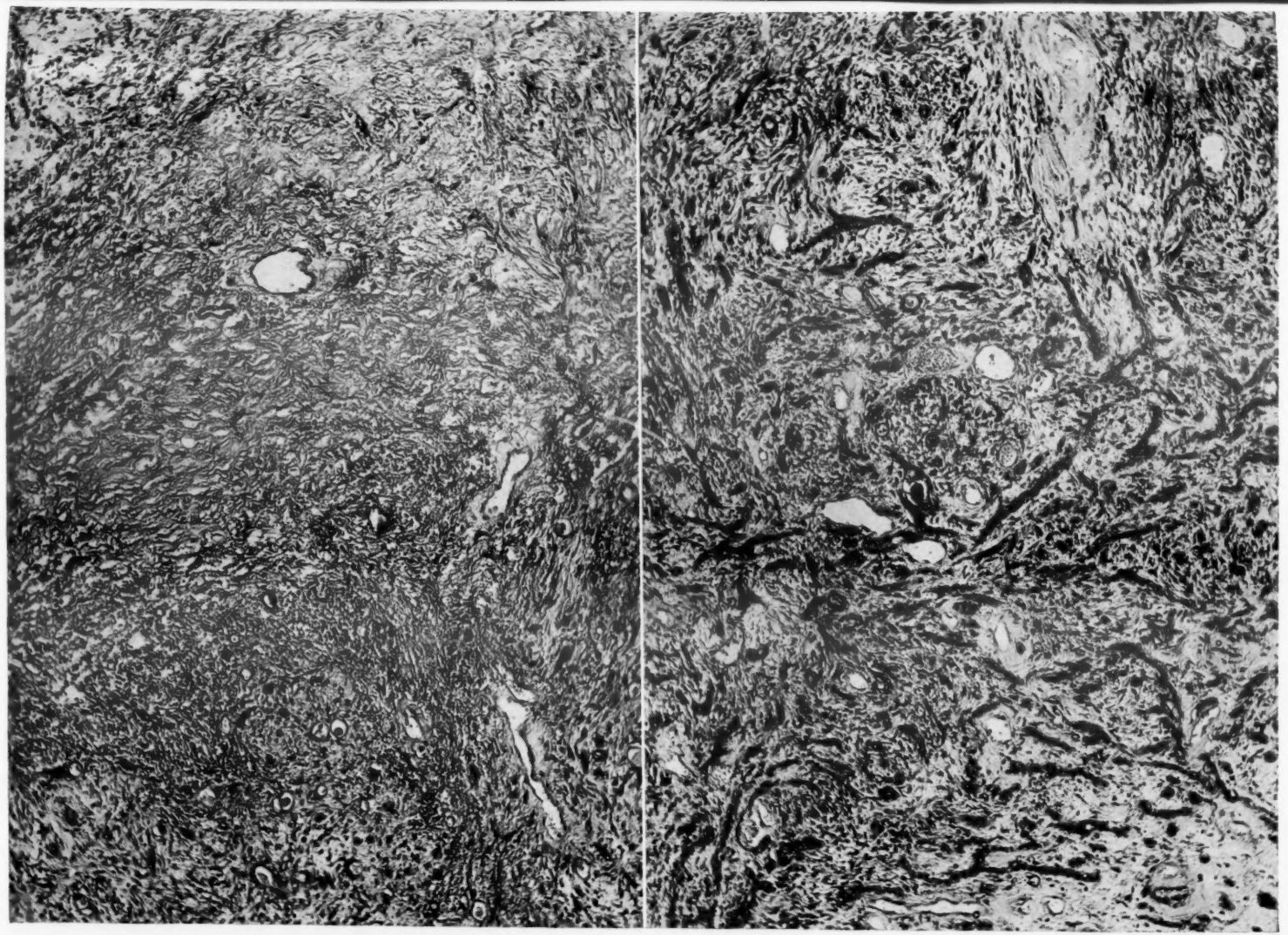
A.

Fig. 2.—Mixed tumor of the skin of the nose. *A*, Sheets of epithelial cells mixed with cartilaginous and mucoid tissue. The epithelium lies on a fibrous connective tissue framework. *B*, Epithelium, occurring in cords and sheets, with formation of cystic spaces. *C*, Gland formation of the epithelium; the latter shows pseudostratified character. *D*, Bone and cartilage ringed by islands of epithelial cells.



B.

A.



C. *D.*

Fig. 3.—Mixed tumor of the scalp. *A,* Perivascular proliferation of cells, which are epithelial in character. *B,* Myxomatous tissue and "pearl" formation of epithelial cells. *C,* Dense fibrous connective tissue permeating substance of the tumor. *D,* Strands and cords of epithelial cells in a fibrous tissue matrix.

stances was trauma specifically involved. Grossly, this singular neoplasm, measuring anywhere from 0.5 cm. to 3 cm. in diameter, is invariably encapsulated with a fine layer of fibrous connective tissue. When surgically excised it can be easily separated from the subcutaneous tissues, but will be found to be inherently attached to the skin, mimicking in this respect the common sebaceous cyst.

The microscopic picture, the only specific method of making an accurate diagnosis, reveals tissue derivatives of both ectoderm and mesoderm. The epithelium may be simple squamous, stratified squamous, or stratified columnar, occurring in cords, sheaths, alveoli, or forming cystic spaces. Occasionally sweat glands and racemose glands can be noted. Mitoses are infrequent (only one instance recorded). The mesodermal tissue usually is fibrous connective tissue, mucoid tissue, cartilage, and bone. Occasionally hyperplasia of the blood vessels occurs. There is no evidence of chronic inflammatory tissue although in several instances lymphocytic infiltration of the tumor proper was recorded.

PRESENTATION OF CASES

CASE 1 (St. E. H., 48-10916).—A 27-year-old white man, a chauffeur, complained of a small mass on the left side of the nose at the level of the nasion of two and one-half years' duration. Although painless, it had suddenly increased in size during the preceding two months. Under intravenous Pentothal analgesia, the tumor was excised in toto. The impression at surgery was that the tumor was a sebaceous cyst. Pathologic report (Slide 1850-1948) was as follows: The specimen measured 1 cm. by 0.7 cm. and consisted of semifirm gray-white tissue. Microscopic examination revealed a complex variety of tissues. There were present sheets of epithelial cells as well as gland formation showing pseudostratified epithelium. There were islands of cartilage and trabeculae of bone. The matrix consisted of connective tissue and pale homogenous mucoid tissue. The diagnosis was mixed tumor of the skin of the nose (Fig. 2).

CASE 2 (St. E. H., 50-263).—A 37-year-old white man, a baker, complained of a "lump" in the back of the head of 12 years' duration; he also had been under therapy for a long-standing hypertension associated with cephalalgia, tinnitus, and left auditory nerve deafness. While under therapy at the hospital for the systemic affliction, the soft painless tumor was excised from the midline of the occipital area of the scalp. At surgery the mass was considered to be a sebaceous cyst. Pathologic report (Slide 53-1950) was as follows: The specimen measured 5 by 3 cm. and consisted of a globoid, semifirm, dark gray-white mass. Microscopic examination revealed both ectodermal and mesodermal elements. The former consisted of recognizable epithelial cells in the form of islands and cords with epithelial "pearl" formation. The mesodermal elements consisted of myxomatous tissue, edematous fibrous tissue, and peri-endothelial epithelial proliferation. The diagnosis was mixed tumor of the scalp (Fig. 3).

SUMMARY

1. Mixed tumors of the skin are a definite pathologic entity, the diagnosis being made on microscopic section.

2. These tumors are benign, usually encapsulated, have a long clinical course, and seldom recur. They may be located in any portion of the body, although the scalp, hand, nose, and fingers are the most common locations.

3. Thirty-four cases of true mixed tumors of the skin have been reviewed in the literature and two additional cases have been presented. Our proposed criteria for diagnosis have served as the basis for their selection.

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EXPERIMENTAL INTRACARDIAC SURGERY WITH EXTRACORPOREAL CIRCULATION

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DURING the past few years numerous publications have appeared in the literature concerning experimental attempts to by-pass the heart in an effort to perform operations within its chambers in a relatively bloodless field. We have been engaged in this experimental approach to intracardiac surgery for the past four years and wish to record our observations.

When first considering the problem of the extracorporeal circulation we felt that it would be wise to relieve the entire heart of its circulation rather than either the right or the left side. The presence of a septal defect between auricles or ventricles renders a bloodless operation through one side of the heart alone impossible. Furthermore, in correcting congenital defects in the heart, it was felt that, if a complete extracorporeal circulation could be maintained, the myocardium would be more completely oxygenated during the operation than at any time previously, since the coronary vessels would be receiving fully oxygenated blood and not a mixed flow of venous and arterial blood. We were also of the opinion that the entire experimental animal should be perfused with oxygenated blood and not the brain only, as has been done elsewhere. This ensures adequate functioning of the kidney, liver, and spinal cord, which otherwise would be rendered relatively avascular for varying periods of time.

We had as our background the experimental work of Gibbon,[1] published in 1939, in which the pulmonary artery in a cat was occluded and the animal was perfused with oxygenated blood. Our early attempts were mainly an effort to develop an approach to the maintenance of an extracorporeal circulation without opening the heart. For this purpose we used the subclavian artery to perfuse the animal, the stream being directed against the aortic valves, which closed; the entire vascular system received oxygenated blood. Venous blood was secured by cannulization of the superior and inferior vena cava and their occlusion on the heart side of the cannulae. We used a Dale-Schuster type of pump which delivered blood into the animal at such a pressure and in such quantity that normal blood pressure was maintained. We found the maintenance of such a pressure in the animal was possible if enough venous blood was returned by way of the venae cavae to equalize the amount being delivered, providing the blood was adequately oxygenated. The next problem, therefore, was one of oxygenation, and we experimented with various artificial oxygenators. It was our experience that the amount of heparin required, the lack of filtering, and the relatively ineffectual oxygenation secured caused our experimental

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animals to die for reasons of bleeding, emboli, and anoxia. Therefore, we abandoned the use of artificial oxygenators and pursued our experiments using a donor dog's lung to oxygenate the blood. With this biological lung we had our first survival of an experimental animal in March, 1949, two years ago.

At first we used the entire lung and gradually lessened this until one lobe, ventilated with 100 per cent oxygen, adequately oxygenated the blood required.

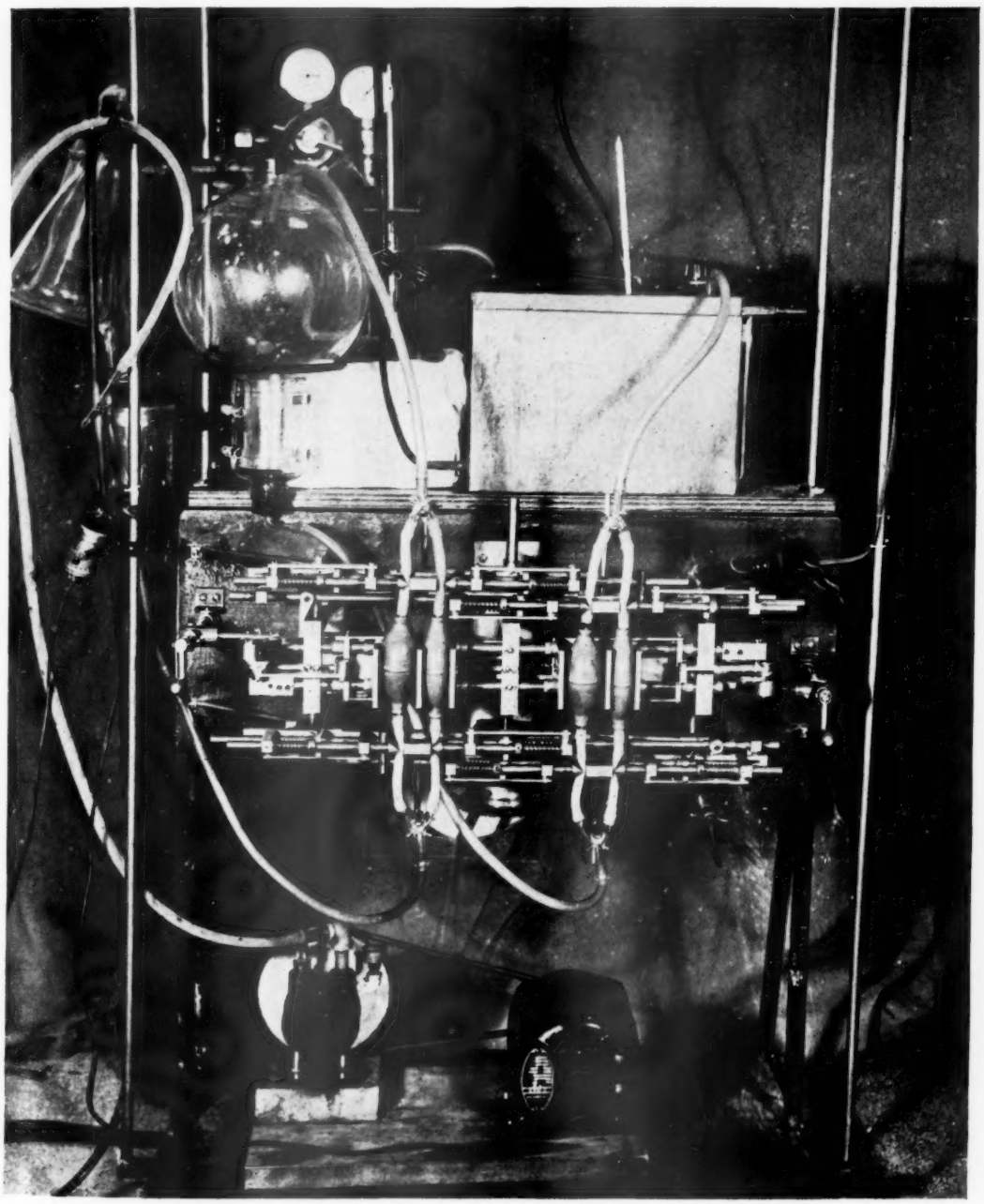

Fig. 1.—Campbell Cowan pump.

We then attempted to use the experimental animal's own lung by cannulating the vein and artery through the right lower lobe and aerating it. Numerous problems of a technical nature were encountered and it was our experience that the lung became quite edematous at the end of our experiment and we were forced to do a lobectomy. In view of this experience, we felt that probably we would be able to secure a donor's lung at autopsy prior to operation and investigated the length of time in which such a lung would be useful post mortem.

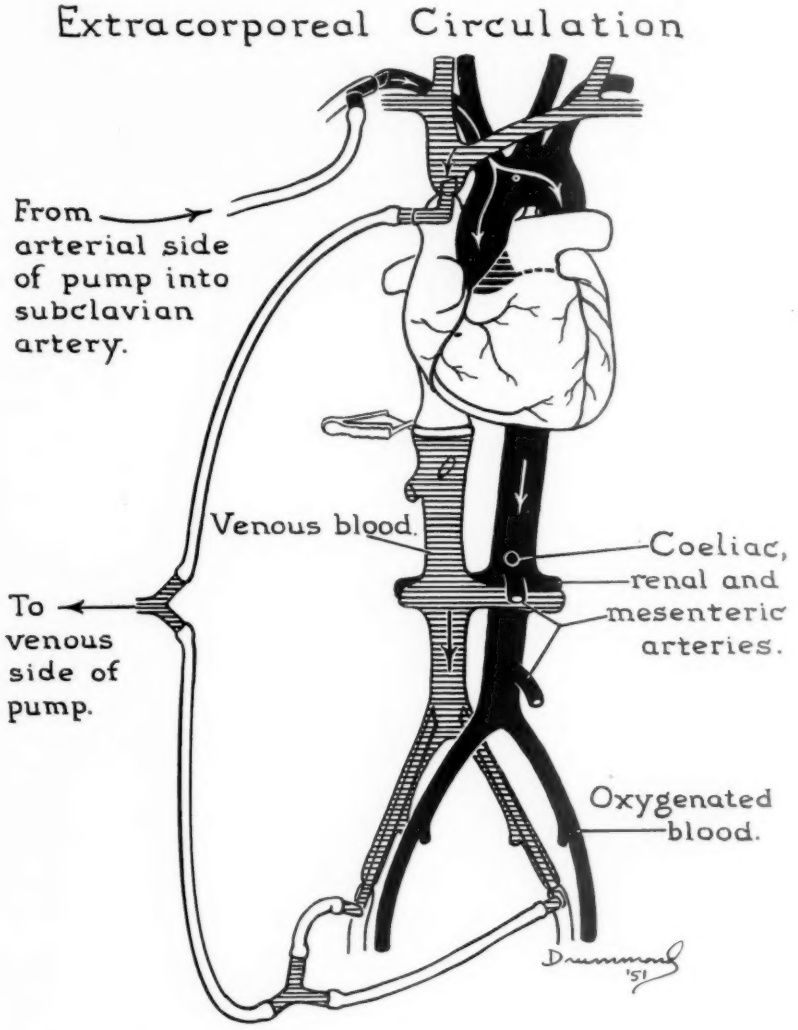

Fig. 2.—Diagrammatic sketch of the technique

In Experiment 3 of our second series, we were able to by-pass the heart successfully for 17 minutes using a lung which had been removed 2½ hours previously. This animal was subsequently sacrificed but was perfectly normal at 2½ months following cardiac by-pass. The advantage of establishing a lung bank is obvious and this possibility is being investigated at the present time. A new type of artificial oxygenator is also being constructed for substitution in the event

of the biological lung becoming edematous in the midst of an operation. Our method improved over the course of time until it was standardized as follows:

Two to three hours before operation a donor dog is bled and the blood is heparinized. The right lower lobe is removed, the bronchus and pulmonary artery are cannulated, and they are then set up on our new type mechanical pump* (Fig. 1). Our experimental dog is then anesthetized and the femoral veins are cannulated. The chest is opened and the azygous vein and subclavian

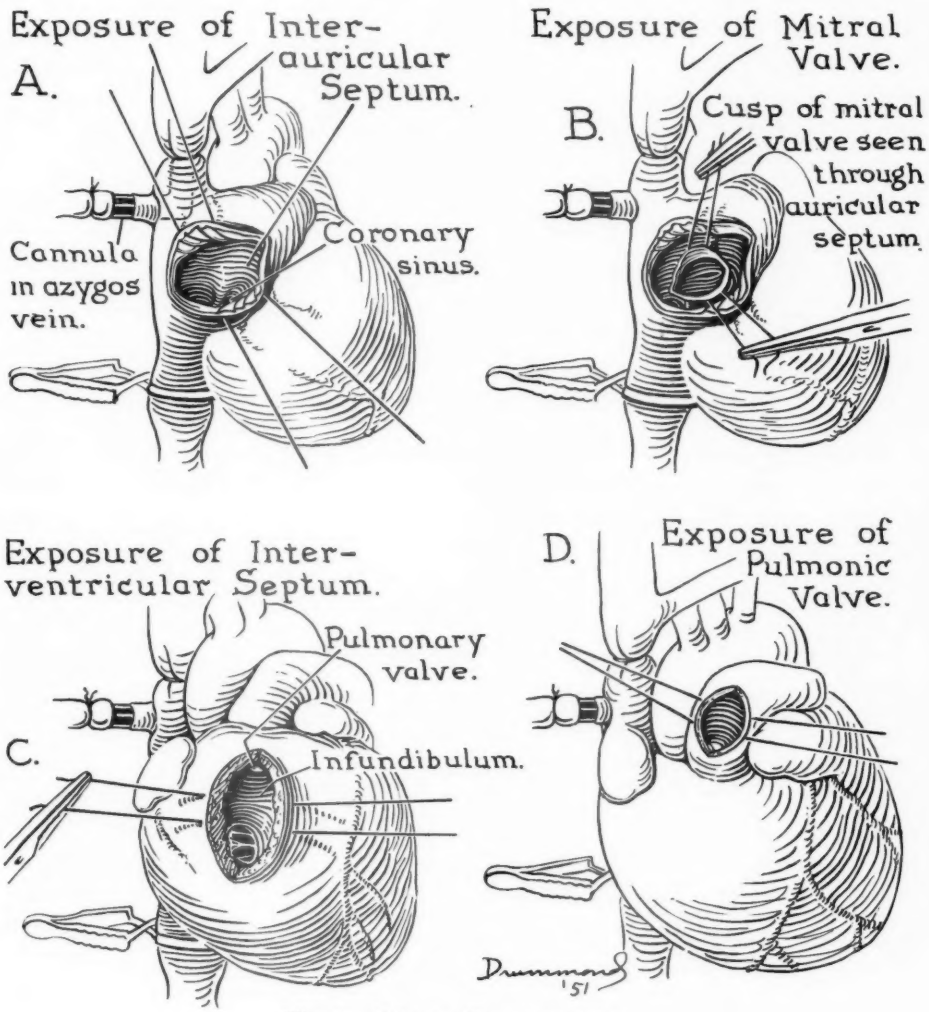

Fig. 3.—Intracardiac exposures.

artery are cannulated, and the venous and arterial sides are connected to the pump. The venae cavae are occluded at their entrance into the right auricle. The venous blood is collected without suction in a reservoir. It is then driven by one set of pumps through the biological lung, which is aerated with oxygen and returned to the animal through another set of pumps at arterial pressure (Fig. 2).

*Made by Mr. Campbell Cowan of the Banting Institute.

When our heart-lung apparatus is stabilized and the animal's blood pressure is normal, the heart is opened. The blood entering the heart from the coronary circulation is removed by suction and returned to the heart-lung preparation. We have carried out numerous operations through the right auricle removing portions of the interauricular septum, repairing artificial defects in the septum, and removing a portion of the mitral valve through the interauricular septum. We have performed valvulotomies on the pulmonic valve through the pulmonary artery and we have opened the right ventricle to visualize the interventricular septum (Fig. 3). Many problems, of course, arise as a result of these intracardiac procedures and many of our dogs succumb to thrombosis or bleeding or secondary effects such as pneumonia and atelectasis.

In our second experimental series, which consisted of 45 operations, we have had ten survivals. These ten survivals represent animals who have lived at least one month or more following operation and are to all intents and purposes normal. Seven animals survived from 2 to 18 days but died of complications arising as a result of intracardiac procedure. We do not consider these as survivals. Seven further animals survived the operation to die one to four hours following intracardiac operation.

In our third series, which will be reported in detail at a later date, we have opened the right ventricle in ten animals, with seven survivals.

This work, aided by a grant from the Banting Foundation, was done in the Department of Experimental Surgery, Banting Institute, University of Toronto. We wish to express our thanks for the unfailing support of Mr. Walter Cowan and for the assistance of Dr. Louis Kennedy and Dr. E. Simmonds.

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ATROPHY OF SARCOMA IN RATS FOLLOWED BY TUMOR IMMUNITY

A Surgical Method for Development of Tumor Immunity in Rats

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With the Technical Assistance of Peter Demchur

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ONE of the principles established by the early studies[13, 16] of cancer in animals is that the regression of a tumor leaves the host resistant to further growth of the same neoplasm. In later studies[9] utilizing animals of inbred strains, it was found that regression of tumors which originated in the host's own strain (native tumors) seldom takes place spontaneously in animals of inbred strains. It was also found that the regression of a transplanted alien strain tumor fails to protect the host from a spontaneous tumor or from the growth of a graft of a tumor which arose in its own strain. It seemed possible, however, that conditions comparable to those occurring in regression might arise during atrophy of a malignant growth provided its blood supply could be occluded sufficiently to bring about atrophy.

Atrophy of a progressively growing tumor suggests several agents which might prove responsible for the resulting immunity. Such an agent might be substances produced during the growth of the malignant tissue which, while unable to combat the progressive growth of an established tumor, might, in its absence, prove sufficiently active to prevent the growth of the comparatively small number of cells which comprise a tumor graft. The agent might be substances formed during the dissolution of tumor tissue, or the engrafted tumor tissue itself might act as an antigen provided its growth was prevented.

It seemed of moment to determine: (1) whether atrophy of a tumor growing in a rat of an inbred strain resulted in the protection of the host from subsequent grafts of tumors which arose in the host's own strain (native tumor); and (2) to determine the antigenic agent responsible for the state of tumor resistance created in the host by this procedure; whether it was substances formed during the growth of the tumor, substances produced during the dissolution of the tumor, or the implanted tumor tissue itself.

METHOD

Three types of experiments were utilized in this study: (1) Atrophy of established tumors brought about by isolation of the tumor in a pocket deprived of blood supply, made by sewing off the tumor in a fold of the loose skin on the side of the host; (2) Implantation of viable tumor tissue into pockets with restricted blood supply prepared in a fold of the loose skin on the right side of a susceptible rat; (3) Ablation of tumors after they had grown for six to eleven days in susceptible rats.

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The rats used were of the Lewis albino and King A inbred strains. Sarcomas which had originated in the strain of the host were used for the transplantations, namely, Lewis sarcoma No. 3 was transplanted into Lewis rats and King a fibrosarcoma No. 231 into King A rats. Grafts of tumor tissue were implanted subcutaneously by means of a trocar (3½ inch, 13 gauge, rustless steel hypodermic needle) midway on the right side and slightly toward the abdominal surface of susceptible rats. Approximately one-half of a trocar full of tumor tissue constituted a tumor graft. The amount of tumor tissue implanted in order to test the resistance of the treated rats (challenge graft) was slightly smaller (one-fifth of a trocar full). Challenge grafts were implanted in the left side of the rat. Four to eight times (one to two trocars full) the amount of tumor tissue used for transplantation was implanted when it was desired to test whether an animal had developed tumor immunity. The operations were performed in groups of five to twelve rats of the same age and usually of the same litter. About the same number of Lewis and King A rats were used in each experiment. The age of the rats and the number of days the tumor had grown varied in the different groups (Table I).

Experiment 1.—When the growing tumor was easily palpable (five to eleven days after implantation) it was drawn into a pocket formed of a fold of the surrounding loose skin of the host and secured there by means of an alligator clamp. The pocket containing the tumor was then sewed off, between the clamp and the body wall of the host, by means of small, closely set back-stitches made with a fine needle and No. 50 to No. 70 thread. If the stitches were small and tight, the blood circulation of the tumor was sufficiently occluded to prevent further growth of the tumor. When moderately large tumors were operated upon, the four large veins and arteries (two from the axillary and two from the inguinal region) which supply tumors located in this region could easily be seen when the fold of shaven skin containing the tumor was held before a bright light. The vessels could then be ligated by means of a thread passed through the skin, around the pair of vessels (vein and artery) and out through the skin. After these large blood vessels were ligated the tumor was confined in a pocket prepared in the loose skin of the rat as described above.

Experiment 2.—A pocket of approximately the same size was prepared in the same manner in a fold of loose skin on the right side of a susceptible rat. A trocar full, in some instances two trocars full, of native tumor tissue was then inserted into the pocket and the viable tumor tissue deposited within the pocket.

Experiment 3.—Tumors, located in the same region, which had grown for six to eleven days in susceptible rats, were confined in similar pockets and then the pockets containing the tumors were excised.

Controls.—Four to ten normal rats of the same age and strain as those used in Experiment 2 were implanted with an equal amount of the same tumor tissue as that inserted into the empty pockets in order to determine the viability of the tumor tissue used. When rats were tested for resistance or for immunity, six to ten normal rats of the same age and strain were implanted with an equal amount of the same tumor tissue to determine the viability of the tumor and the susceptibility of rats of the age used in the tests.

TABLE I. DEVELOPMENT OF TUMOR-IMMUNITY IN RATS FOLLOWING INHIBITION OF TUMOR GROWTH

NUMBER RATS USED	AGE OF RATS (DAYS)	NUMBER OF DAYS TUMOR HAD GROWN IN HOST BEFORE OPERATION	NUMBER OF TUMORS THAT GREW	NEGATIVE RATS TESTED FOR RESISTANCE	NUMBER OF RATS RESISTANT
		Experiment 1. Atrophy of Established Tumors			
7*	40	6	1	6	5
8*	50	7	0	8	7
6*	50	6	2	4	4
6*	60	10	1	5	5
4	35	5	0	4	4
8	40	8	0	8	6
7	35	5	0	7	5
8	60	11	0	8	8
54			4	50	44
		Experiment 2. Restriction of Growth of Engrafted Tumor Tissue			
10*	50	graft	3	7	0
12*	40	graft	0	12	2
8	35	graft	1	7	4
7	30	graft	2	5	0
13	50	graft	2	11	1
50			8	42	7
		Experiment 3. Ablation of Established Tumors			
8*	40	6	0	8	1
3*	50	8	0	8	0
3	60	10	0	3	0
6	90	7	0	6	1
7	60	11	0	7	0
32			0	32	2
		Controls			
200	30 to 90	graft	200	0	0

*The litters of Lewis rats implanted with sarcoma No. 3 are starred. The others are litters of inbred King A rats, implanted with sarcoma No. 231. The results obtained were the same regardless of whether Lewis rats and native sarcoma No. 3 or King A rats and native sarcoma No. 231 were used.

RESULTS

The results given in Table I show that only four of the tumors deprived of blood supply and isolated in pockets in the loose skin of the host continued to grow in the fifty-four rats operated upon in Experiment 1. Later examination of these rats disclosed that one of the blood vessels leading into the tumor had escaped occlusion and served as a source of blood supply for the growing tumor. In six of the rats, the pocket containing the tumor came off within one to two days, leaving the site completely healed. In the remaining forty-four rats, the tumor disappeared from the pocket within four to eight days; the pocket became dry and came off some days later. The fifty tumor-free rats were given a challenge graft one month after the operation. Six of them developed tumors. These six rats were the ones from which the pockets containing the tumors came off shortly after the operation. The other forty-four rats remained free from tumor growths for thirty or more days. At the end of this time they were implanted with large amounts of tumor tissue to test whether they had developed tumor immunity. The grafts failed to grow and the rats remained free from tumors as long as they were kept under observation (six weeks to 6 months).

Experiment 2.—The viable tumor tissue implanted into the sewed-off pockets grew in eight of the fifty rats operated upon in Experiment 2. It was later found that an unoccluded blood vessel had formed a source of blood supply for the growing tumor tissue. Metastatic growths were present in the lungs and draining lymph nodes of three of the rats in which the tumors grew in the confined space of the sewed-off pocket. It seemed probable that pressure exerted at the time of implantation had forced a few cells into a blood vessel or a lymph space in the region of the stitches. The implanted viable tumor tissue failed to grow within the pockets in the other forty-two rats and the pockets remained attached to the host for some time before they became dry and came off. The forty-two tumor-free rats which resulted in Experiment 2 were implanted with a challenge graft of viable tumor tissue one month after the operation. The tumor tissue grew in thirty-five of the forty-two rats. One to two months later the seven tumor-resistant rats were implanted with a large amount of tumor tissue. These grafts failed to grow, showing that the hosts had developed tumor immunity.

Experiment 3.—The thirty-two rats from which established growing tumors were excised recovered and no recurrence of tumor growth took place. When tested for tumor resistance, the challenge graft grew in thirty of the operated rats. The two rats which proved to be resistant to the challenge graft later died from tumors which developed from the large grafts implanted in order to test their immunity.

Controls.—The tumor grafts grew in all (more than 200) of the control animals, showing that the tumor tissue used for the challenge grafts and for the immunity tests were viable and that untreated rats of the inbred strains used were susceptible to the growth of grafts of the native tumors implanted in the experiments.

The fifty-one tumor-immune rats which resulted from Experiments 1 and 2 remained free from tumor growth as long as they were kept under observation (six weeks to six months). Six weeks after the experiments were completed, ten of the rats were autopsied and found to be free from metastatic growth. Twenty-nine of the remaining rats were implanted about six months later with two trocars full of viable tumor tissue and found to be still resistant to tumor growth. The remaining twelve rats lived normal lives, bore offspring, and remained free from tumor growth until they eventually succumbed to old age.

Rats of two strictly inbred strains and sarcomas which originated in the host's own strain were utilized in these experiments. It may be concluded, therefore, that the state of resistance which developed in these animals is one of immunity from native sarcomas, not a resistance to foreign tumor tissue as has been described by earlier investigators.[1, 13, 16]

DISCUSSION

Regression of tumors which arose in the host's own strain seldom takes place spontaneously in rats and mice of inbred strains. Few investigators have utilized animals of inbred strains and neoplasms which arose in the host's own strain in studies concerning regression of tumors or development of tumor immunity.

Lewisohn, Leuchtenberger, Leuchtenberger, Laszlo, and Dische[12] studied regression of spontaneous mammary gland carcinoma following intravenous injections of extract of spleen and yeast in mice. These investigators, however, were interested in the cure of cancer and not in the development of immunity. Gross[6] utilized C_3H inbred mice and a sarcoma which developed in a mouse of the same strain. By intracutaneous injections of a dilute suspension of malignant cells, he was able to produce small tumors which regressed spontaneously in a number of the treated mice. When the tumor-free mice were later implanted with grafts of viable sarcoma cells, a small number of the mice proved to be resistant to further growth of native tumor tissue. Aptekman, Lewis, and King[2] and Lewis, King, Aptekman, and Seibert[10] found that intratumoral injections of an alcoholic extract of tumor tissue prepared from mouse, rat, or human neoplasms brought about resorption of sarcomas followed by immunity in 100 per cent of the treated rats. Lewis and Aptekman[11] claimed that subcutaneous injections of Adrenalin into the neighborhood of tumors growing in rats restricted their blood supply sufficiently to cause regression of the treated tumors and development of immunity in the hosts.

The results obtained from the present experiments show that atrophy of a sarcoma which had grown progressively in a susceptible rat of an inbred strain for five to eleven days protected the host from growth of subsequent grafts of sarcoma which originated in the host's own strain (native tumor). Native tumors undergoing atrophy due to lack of adequate blood supply produced in the host some substance which tended to prevent growth of subsequent grafts of malignant tissue to which untreated rats of the same strain were susceptible. Absorption of implanted tumor tissue which was prevented from growing into a sarcoma by restriction of its blood supply and substances formed by the active growth of a sarcoma for five to eleven days prior to its excision failed to protect the host from growth of subsequent grafts of native sarcomas.

Various changes which take place in animals and human beings during the growth of a neoplasm have been described.[3, 4, 5, 7, 8, 14, 15] It has been shown that the majority of these changes subside after the removal of the malignant growth, followed by the return of the host to a comparatively normal state. It is, therefore, not surprising to find that substances produced during the growth of a tumor fail to protect the host from growth of grafts of malignant tissue implanted some time after the excision of an established tumor.

There is a wide divergence in conditions which occur in animals following transplantation of an alien strain tumor and a native sarcoma. This is shown by the fact that growth of a graft of foreign tumor tissue for as little as five days prior to excision brings about the production of substances which protect the host from further growth of the same foreign tumor tissue but not from native neoplasms.[1, 9, 13, 16]

With the exception of the results obtained from the polarographic studies of the serum of immunized rats,[4] little is known of the physiologic state of animals immunized against native tumor growth. The surgical procedure utilized in the present experiments, which results in the dissolution and absorption of established neoplasms, furnishes a method for the study not only of changes

which take place in the host, but also of those which occur in the tumor tissue during atrophy and development of tumor immunity. It is hoped that studies now in progress on the antigenicity of tumor tissue removed at different stages during atrophy will help toward a clearer understanding of the conditions which take place in these rats during the development of tumor immunity.

SUMMARY

Isolation of a growing rat sarcoma in a pocket deprived of adequate blood supply, sewed off in a fold of the loose skin of the host, resulted in atrophy of the restricted tumor within four to eight days.

Atrophy of a tumor which had grown progressively in a susceptible rat for five to eleven days protected the host from growth of subsequent grafts of tumor tissue.

The development of tumor immunity in the treated rat apparently resulted from absorption of substances formed or conditions which arose during atrophy of the tumor. The absorption of implanted tumor tissue which was prevented from growing into a tumor by restriction of its blood supply and the active growth of a tumor for six to eleven days prior to its excision failed to induce a state of resistance to growth of subsequent grafts of tumor tissue in the treated animals.

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Case Reports

ACUTE PANCREATITIS FOLLOWING TRANSAMPULLARY BILIARY DRAINAGE

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THIS report presents the unusual occurrence of obstruction of the ostium of the duct of Wirsung by a long T tube, followed by fatal necrotizing pancreatitis. No previous report of any similar case has been noted by the participants in this study. Cattell,[1] in 1948, reported encrusting in the tube limbs as the only complication encountered in the use of the long T tube at the Lahey Clinic for the previous ten-year period. Subsequently, Warren[2] stated that no complication such as the one here reported occurred in the Lahey Clinic series. The pancreatitis found at autopsy of this patient was probably a direct consequence of the use of the transampullary tube, but the possibility of its having been coincidental cannot be excluded. The following case is presented to indicate this development as a possible danger attendant upon the use of the long T tube.

CASE REPORT

History.—A 68-year-old white man, a veteran, was admitted to the Medical Service of the Wadsworth General Hospital on May 30, 1950, with jaundice of ten days' duration. For approximately two weeks prior to entry, he had slight anorexia, and nausea following meals. Ten days before admission, he became icteric and noted clay-colored stools and dark urine.

Physical Examination.—The patient was a well-developed, well-nourished, markedly icteric white man in no acute distress. The heart and lungs were normal. The abdomen was soft and nontender and during deep inspiration the liver edge was palpable in the anterior axillary line, four fingerbreadths below the costal margin. The edge of the liver was firm, smooth, and nontender. The spleen was not palpable.

Laboratory Data.—Tests on entry revealed a normal blood count. The urine concentrated to 1.016 and contained a trace of albumin and 5 to 8 white cells per high power field. X-ray examination of the abdomen revealed a faint shadow measuring approximately 2 cm. in diameter in the region of the gall bladder. A second small calcific density was seen just opposite the body of L_1 and just to the right of the vertebral column. On three occasions urinary urobilinogen levels were elevated. Evidence of impaired liver function was demonstrated by a falling serum cholesterol and ester fraction, and by elevated thymol flocculation and turbidity values. Alkaline phosphatase was 6.6 units. The icterus index progressively increased, and the prothrombin time decreased. The stool guaiac test was positive. An extrahepatic biliary obstruction was considered the most likely diagnosis, and the etiologic agent was presumed to be a stone.

Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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Operation.—On June 21, 1950, a laparotomy was performed. The liver was enlarged and firm and presented a blunt edge. The surface was a deep brown green and showed fine reticular scarring. The gall bladder was shrunken and scarred and contained one large stone which measured 3 cm. in its greatest dimension. This stone appeared to be composed of an aggregate of multiple small cholesterol stones. Some edema and inflammatory reaction were noted around the common duct, and an area of induration approximately 1 cm. in diameter could be felt in the region of the ampulla of Vater. A slightly denser area was palpable in the head of the pancreas 2 to 3 cm. to the left of the ampulla. The common duct was normal in size and contained a small amount of thin bile. The duct appeared to be free of stones, and the ampulla could be probed readily. Because of the persistence of the area of induration, a longitudinal duodenal incision was used to expose the papilla of Vater. This was found to be patent and without evidence of tumor or stone in its lumen. A soft rubber T tube was then prepared by splitting its horizontal arm longitudinally throughout its length. It was placed in the common duct with the distal arm leading through the ampulla into the duodenum. The gall bladder and its contained stone were removed. A biopsy specimen of the liver was taken from near the falciform ligament.

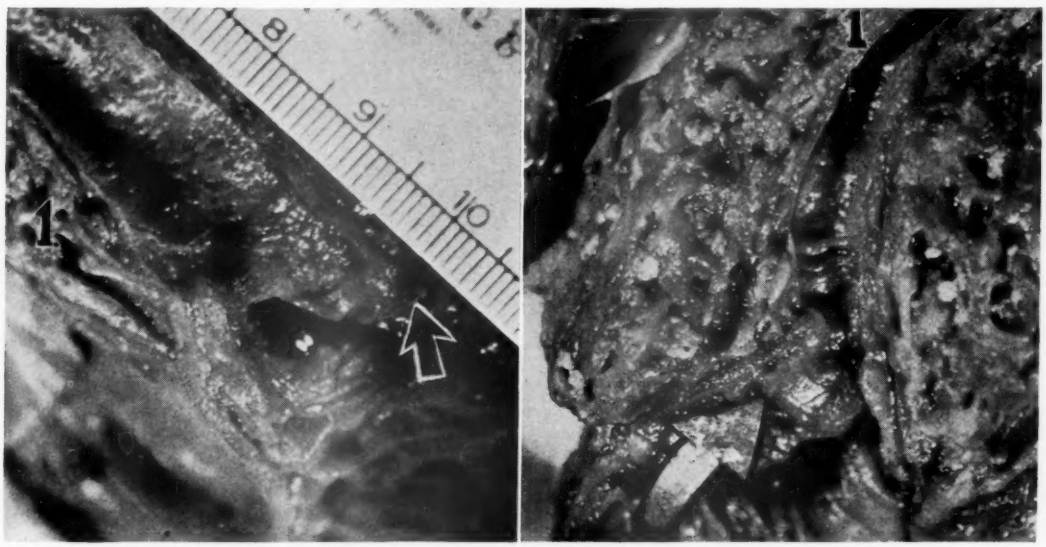
Postoperative Course.—The patient's course for the first week appeared satisfactory, the temperature not rising above 99.2° F. (rectal). Gastric suction was discontinued on the fourth day and a soft diet instituted. He received dihydrostreptomycin prophylactically. The common duct catheter drained between 200 c.c. and 500 c.c. of thin, pale bile per day. The jaundice did not subside, however, and on the eighth postoperative day a blood count revealed 52,400 white blood cells with 79 per cent segmented neutrophils, 11 per cent band forms, and 3 per cent metamyelocytes. No obvious cause for this elevation was discernible. On the twelfth postoperative day, the drainage tract region was probed under local anesthesia and 30 to 40 c.c. of thin, grayish fluid were removed without alleviation of the symptoms. The patient then complained of midepigastric boring pain and mild backache. Fourteen days postoperatively he developed oliguria. The blood urea nitrogen was 70 mg. per 100 c.c., and one day later he became anuric. Attempts to restore the electrolyte balance were limited by the anuria and by the appearance of edema. The blood sodium chloride fell to 83.6 meq. per liter (484 mg. per cent) and the carbon dioxide combining power to 4.3 meq. per liter (10 volumes per cent). The patient gradually became comatose and died on the sixteenth postoperative day.

Autopsy Report.—Externally, a deep golden icterus and surgical incisions on the abdomen were noted. The operative site and the opposing surfaces of the omentum, liver, and anterior abdominal wall were coated by a thin, bloodstained, fibrinopurulent exudate. No free fluids could be found. The rubber T-tube catheter entered the common bile duct anteriorly 3 cm. distal to the point of origin of the common hepatic duct. There was no evidence of tissue reaction nor of leakage of bile at this site. The process of slitting the horizontal arm of the T tube had "sprung" the tube somewhat. The tube was removed with difficulty from the mucosa of the bile ducts to which it seemed to be adherent. It had induced a slight dilatation of these ducts. The common bile duct measured 1.4 cm. in circumference and was anomalous in its course. Its distal third first passed posteriorly and then curved anteriorly to end at the ampulla of Vater. The arc of this curve subtended an angle of 40 degrees. The distal end of the common duct was ringed by pancreas which possibly represented the nodule palpated at the time of operation (Fig. 1, *A*). The ostium of the common pancreatic duct (Fig. 2, *1*) was an oval-shaped, thin-lipped opening on the posterior wall of the common bile duct at a point 1 cm. proximal to the overhanging lip of the ampulla of Vater (Fig. 2, *A*).

Sections of the posterior wall of the distal end of the common bile duct revealed mucosal compression necrosis (Fig. 2, *A*). The mucosal epithelium was sloughed and its surface replaced by parallel lines of compressed subepithelial connective tissue, fibrin and chronic inflammatory cells (Fig. 2, *B*). These cells were found throughout the thickness of the wall of the common bile duct. Further evidence of mural compression by the rubber catheter was

discerned by examination of the submucosal glands of the common bile duct. The excretory ducts of the glands were compressed in a line parallel to the mucosa, and their secretory alveoli were widely distended (Fig. 2, *A*).

The common pancreatic duct was narrow at its juncture with the bile duct (Fig. 1, *B*), but was dilated considerably, proximally. No calculi were found. The duct of Santorini entered the duodenum 3 cm. proximal to the ampulla of Vater. However, dissection of this duct failed to demonstrate any grossly visible communication with the dilated duct of Wirsung. The head and neck of the pancreas were swollen and their limiting capsule was tense. There was no reaction upon the surface of the pancreas. When sectioned, the entire head and neck appeared to be converted into a series of honey-combed cavities filled with friable, dirty gray and white, granular, necrotic debris. These cavities measured up to 0.3 cm. in diameter (Fig. 1, *B*). Some of these were multilocular, whereas others seemed to communicate with one another. Between these, the residual pancreatic parenchyma was barely recognizable because of the edema and minute degenerative changes that were grossly visible. The body and tail of the pancreas showed similar, though fewer, foci of pancreatic necrosis. Microscopic study revealed dilatation of even the small pancreatic duct radicles, some of which exhibited eccentric mural necrosis and surrounding typical pancreatic enzyme necrosis. The necrotic cavities were filled with sloughed pancreas and fatty acid soaps and were lined by an acute and subacute inflammatory process. In some foci of necrosis, calcium salts were already precipitating from the debris.



A. *B.*

Fig. 1.—*A*, Arrow points to lip of ampulla of Vater. Note arched curve of distal end of dilated common bile duct. Note at (*1*) sleeve of periductal pancreas. Note metal probe extending through opened thin-lipped ostium of main pancreatic duct. *B*, Arrow points to lip of ampulla of Vater. Note at (*1*) the narrowed proximal end of pancreatic duct and its dilated distal portions. Note the honey-combed necrotic head of pancreas.

The liver weighed 1,200 grams. It was smaller and softer than normal and was a dusky blue brown. Its capsule was smooth and its edge sharp. It cut with ease and, when it was sectioned, the parenchyma retracted beneath the Glisson's capsule. The parenchymal markings were obscured. Microscopically the pattern (as in the surgical biopsy) suggested subacute smouldering hepatitis and was morphologically similar to the pattern seen in infectious hepatitis. The kidneys were slightly enlarged and together weighed 480 grams. They were slightly granular. Microscopically, the tubular degenerative changes along with icteric cast deposition were morphologically similar to those described in severe "icterus nephrosis."

The microscopic findings were as follows: (1) subacute hepatitis, (2) postoperative cholecystectomy, (3) T-tube (long) drainage of bile duct, (4) compression (mural) of bile ducts and pancreatic duct ostium, (5) acute pancreatic necrosis, (6) bilateral bronchopneumonia with microabscesses of the lung, and (7) an occult adenocarcinoma of the prostate gland.

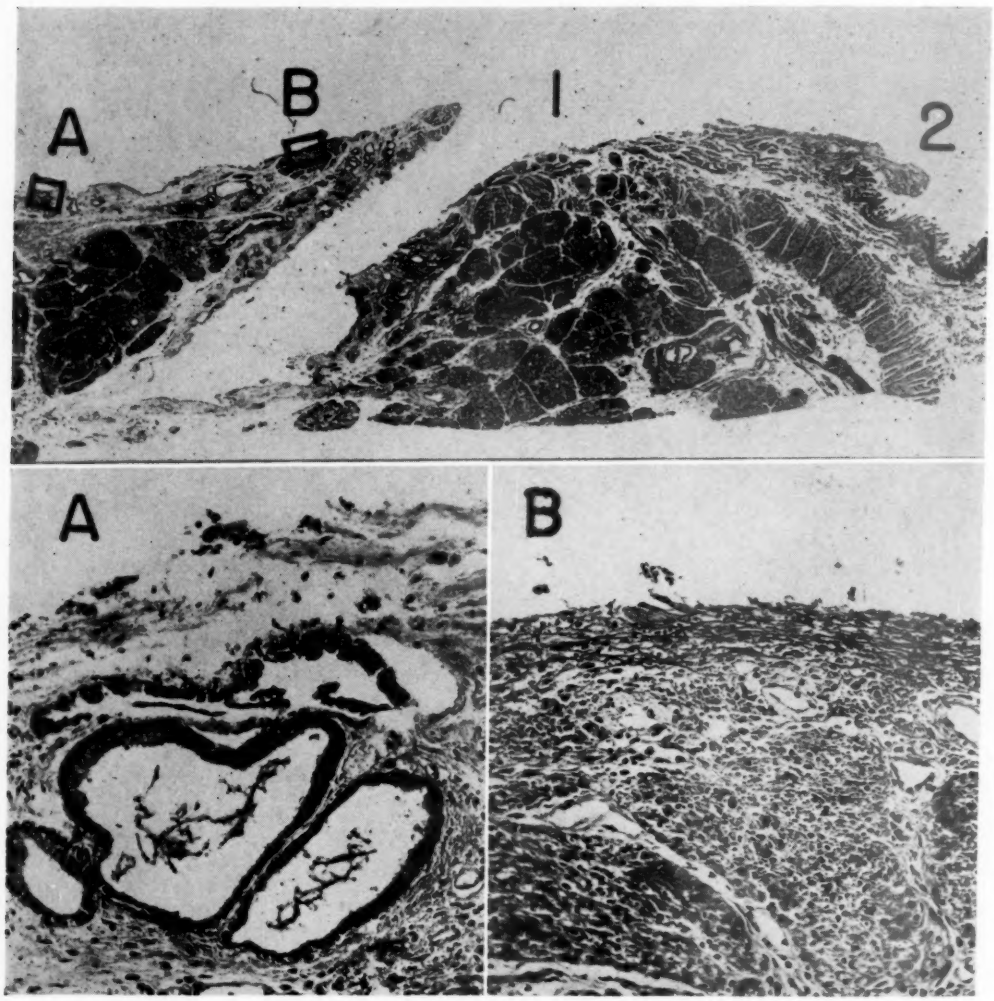


Fig. 2.—*Upper:* (*1*) ostium of common pancreatic duct, and (*2*) lip of ampulla of Vater. *A* and *B* represent sites of higher power photo micrographs of common bile duct.

Lower: *A*, Note sloughing necrosis of surface mucosa and compression of excretory portions and dilatation of secretory portions of submucosal glands. *B*, Note laminated compressed mucosal surface containing fibrin and mural chronic inflammatory cells.

DISCUSSION

Approximately six days after operation, the patient's course began to show a change which was manifested mainly by the leucocytosis. In retrospect, this change appears to have represented the onset of the pancreatitis. No clear answer can be given to the question of the cause of pancreatitis. It is generally agreed that partial or complete obstruction in the ampulla is one causative factor, and that retrojection of bile possibly is a contributory

etiologic agent. Complete obstruction of the pancreatic duct by ligation, however, does not regularly cause pancreatitis, nor does the presence of bile in the pancreatic duct alone cause it. It seems likely that stasis due to partial obstruction, associated with some factor such as activation of pancreatic enzymes by retrojected bile, may be effective in producing pancreatitis.

In this particular instance, the pressure of the arched T tube against the common wall of the pancreatic and bile ducts apparently permitted the development of pancreatic stasis. Fitting snugly as it did into the distal ampulla, moreover, it may have allowed some bile to be mixed with pancreatic secretions.

In order to obtain information concerning the frequency with which such an obstruction could occur, the porta hepatis and the ampullary and pancreatic ductile systems were carefully dissected in the course of performing 45 autopsies. In 57.7 per cent of the specimens, the duct of Wirsung entered the common duct 1 mm. or more proximal to the lip of the papilla of Vater. This entrance was invariably in a postero-medial position and at an acute angle (Fig. 2). In each specimen the common wall of the common and pancreatic ducts at the ostium of the latter was extremely thin and membranous. This general anatomic pattern is confirmed by previous work of Cameron and Noble,[3] who demonstrated reflux of bile in 66 per cent of a series of unfixed post-mortem specimens in which the ampulla was occluded at its distal end. Howard and Jones[4] reported a series of 150 autopsies in which they demonstrated that such a reflux was possible in 54 per cent.

Because of the narrow caliber of the normal ampulla and because of the snugness with which a tube lies within it, it seems likely that the occlusion would occur in a significant number of cases thus intubated.

TABLE I. DISTANCE OF OSTIUM OF DUCT OF WIRSUNG FROM EDGE OF PAPILLA OF VATER IN 45 FRESHLY EMBALMED SPECIMENS FOR AUTOPSY

LOCATION	NUMBER OF CASES	PER CENT
No duct of Wirsung	1	2.2
Outside ampulla	6	13.3
At edge of papilla	12	26.6
1 mm. proximal to papilla edge	2	4.4
2 mm. proximal to papilla edge	3	6.6
3 mm. proximal to papilla edge	7	16.6
4 mm. proximal to papilla edge	4	8.8
5 mm. proximal to papilla edge	4	8.8
6 mm. proximal to papilla edge	0	0.0
7 mm. proximal to papilla edge	2	4.4
8 mm. proximal to papilla edge	1	2.2
9 mm. proximal to papilla edge	2	4.4
15 mm. proximal to papilla edge	1	2.2
Total	45	

Patent communication in this case between the duct of Wirsung and the duct of Santorini could not be demonstrated. Howard and Jones[4] observed a patent duct of Santorini and a communication between the ducts of Santorini and Wirsung in 54 (46 per cent) of 150 autopsies. If obstruction is accepted

as a factor in the causation of pancreatitis, the lack of this alternate channel for decompressing the ducts must certainly play an important role in the development of pancreatitis.

If this configuration alone were the cause of the obstruction and thus of the pancreatitis, the complication would be expected to develop more frequently in the presence of a long T tube. Another less well-defined factor, probably referable to the activation of the pancreatic enzymes, certainly should be considered.

Several factors, therefore, probably operated to produce this untoward complication of so well-established and useful a technique as transampullary drainage: (1) The main pancreatic duct entered the common duct at an acute angle and within the ampulla; (2) the course of the common duct was such that the T tube was thrust against the common wall between the pancreatic and biliary ducts, occluding the former; (3) the duct of Santorini did not communicate with the duct of Wirsung.

SUMMARY

1. The clinical history and autopsy findings of a case of fatal necrotizing pancreatitis are presented, in which the pancreatitis followed transampullary biliary drainage through a long T tube.

2. The possibility is discussed that obstruction of the ostium of the duct of Wirsung by the distal limb of the T tube led to the pancreatitis.

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PERFORATION OF DUODENAL STUMP FIVE AND ONE-HALF MONTHS AFTER SUBTOTAL GASTRECTOMY

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SINCE the advent of gastric resection the problem of perforated or blown-out stump has confronted the surgeon. Many ideas have been proposed as to the causative factor in perforated or blown-out stumps; such as circulatory embarrassment, neurocirculatory, intraduodenal pressure; mechanical obstruction at or near the gastrojejunal anastomosis.

There is a case reported from Argentina[1] with rupture of the duodenal stump ten and one-half months following subtotal gastrectomy. However, in this instance there had been leakage from the duodenum immediately postoperatively, and on several occasions prior to the time the perforation was proved by operation.

We are presenting a report of a case of perforation of the duodenal stump five and one-half months after subtotal gastrectomy.

CASE REPORT

This was the first Bellevue Hospital admission of this 43-year-old white man.

Past History.—Following a five-year history of epigastric burning, the patient was found to have a gastric ulcer. Five and one-half months before admission (November, 1948) subtotal gastric resection was performed at Halloran Hospital. By personal communication we were informed by the surgeon that at least one-half of the stomach was removed and the entire ulcer, which was prepyloric, was removed with the specimen. An anterior Pólya gastrojejunostomy was performed.

Present Illness.—Two hours before admission, one and one-half hours after eating, this patient had a sudden onset of dyspnea and shortness of breath. One hour later he had sudden severe epigastric pain which persisted to the time of admission, and this was immediately followed by vomiting of bile-stained food. The epigastric pain (of increasing severity) persisted.

Admission Physical Examination.—The patient was a thin, asthenic man lying on his right side complaining of severe epigastric pain and vomiting bile-stained fluid continuously.

Blood pressure was 120/78, temperature 97.4° F., Respiration 20, and Pulse 80. The tongue was moderately dry, not coated. The lungs were clear to auscultation and resonant on percussion. The cardiovascular system was not remarkable. The abdomen was soft, nonrigid. A small protuberance, approximately 4 cm. in diameter, was noticed just to the left of the umbilicus. This area and the epigastrium were moderately tender. Both areas were easily compressible. A recently healed right upper rectus incision was present. The remainder of the examination was essentially negative.

Laboratory.—The white blood cell count was 15,300, hemoglobin 15.5 Gm. The urine was clear yellow, with a specific gravity of 1.025, acid and no sugar or albumin. Microscopical examination was negative for cells or casts. A flat plate of the abdomen showed no air under the diaphragm and no masses or calcifications. A chest plate showed heart and lungs to be normal.

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Course.—A Levine tube was passed and the stomach was aspirated. The patient was maintained on suction. One hour later the mass to the left of the umbilicus disappeared. Thereafter the patient was more comfortable. Pain became localized to the right upper quadrant and the right epigastrium. At 6 A.M. the following morning, 13 hours after admission, the pulse rose to 140 to 160 and the blood pressure became unobtainable. The patient had already received 1,000 c.c. of 5 per cent glucose in DW; at this time 500 c.c. of whole blood were given. By 9 A.M. the blood pressure had risen to 90/60 and in the next 40 minutes it rose to 100/60. At this time the patient was taken to the operating room.

Operation.—After the induction of general anesthesia the abdomen was entered through the old right upper rectus incision. On entering the lesser sac a large amount of intestinal fluid of semipurulent nature was encountered and cultured. Throughout the operation this fluid was in abundance, mostly in the subdiaphragmatic regions and the lesser sac. Multiple adhesions were divided throughout the lesser sac, exposing its depths. There was no perforation visible in this region. The pancreas was visualized and found to be normal and the gastroenterostomy anastomosis was found to be intact. The liver was freed from its adhesions to the stomach and colon and the gall bladder was visualized and found to be normal. The greater omentum was thickened and densely adherent over the duodenal stump and the hepatic flexure of the colon. The omentum was divided, liberating a large amount of biliary fluid, which had been encapsulated under the omentum, around the duodenal stump. On the anterior wall of the stump a small necrotic area, about 0.5 cm. in diameter, was visualized, in the center of which was a very minute hole which was exuding biliary fluid. This hole was plicated with one through and through 00 chromic catgut suture and three overlapping Lembert sutures of the same material. A cigarette drain was placed adjacent to the plicated area and brought out through the lower end of the wound. The peritoneum was closed with a continuous 00 chromic catgut suture, the superficial fascia with interrupted sutures of similar material. The subcutaneous tissues were approximated with several 00 plain catgut sutures and the skin was closed with interrupted silk mattress sutures. The patient received 1,000 c.c. of whole blood during the procedure. Blood pressure at the beginning of the operation was 60/40 and for part of the time during the procedure was not detectable. At the time he was returned to the ward the pressure was 90/60 and his condition considered poor. A Levine tube was inserted.

Postoperative Course.—Immediately after his return to the ward, he had a shaking chill. He was given blankets and hot water bottles and placed on shock blocks. The blood pressure had risen to 105/65 and the pulse was full and regular at 90 per minute shortly thereafter. The patient had completely reacted and seemed to be making satisfactory progress, so the shock blocks were removed. At 9 P.M. the same day, the patient complained of dyspnea and suddenly went into shock, at which time the blood pressure was 50/30. He was warm, perspiring profusely, and his skin had an orange-red flush. He was again given 500 c.c. of blood, but despite this the blood pressure was never higher than 70/50. The pulse fluctuated widely between 100 and 160. One hour later he voided 90 c.c. of urine. This was reddish-brown and on microscopic examination was seen to contain numerous hemoglobin casts. It was thought that the patient had developed lower nephron nephrosis as a result of an incompatible blood transfusion and the transfusion was discontinued. Neosynephrine, 1.0 c.c., was given intravenously without avail. The blood pressure through the night varied from 50/30 to 70/50 and the pulse remained rapid and weak. On the basis of a medical consultation the next morning, Doca was given intramuscularly. Despite this and the administration of plasma and nasal oxygen the blood pressure continued to fall. At no time did he manifest any signs of cardiac or respiratory complication. An electrocardiogram done by the medical consultant failed to reveal any abnormalities. The pulse and blood pressure remained unobtainable for the last six hours before he died. Complete studies of all blood used for transfusion on this patient by Dr. Weiner's laboratory revealed no evidence of incompatibility.

*Autopsy.**—

Abdominal Cavity: On opening the abdominal cavity approximately 900 c.c. of cloudy nonfoul bile-stained fluid was seen. The peritoneal surface had fibrin deposited throughout

*Reported by Dr. Sikoloff and Dr. Hindman.

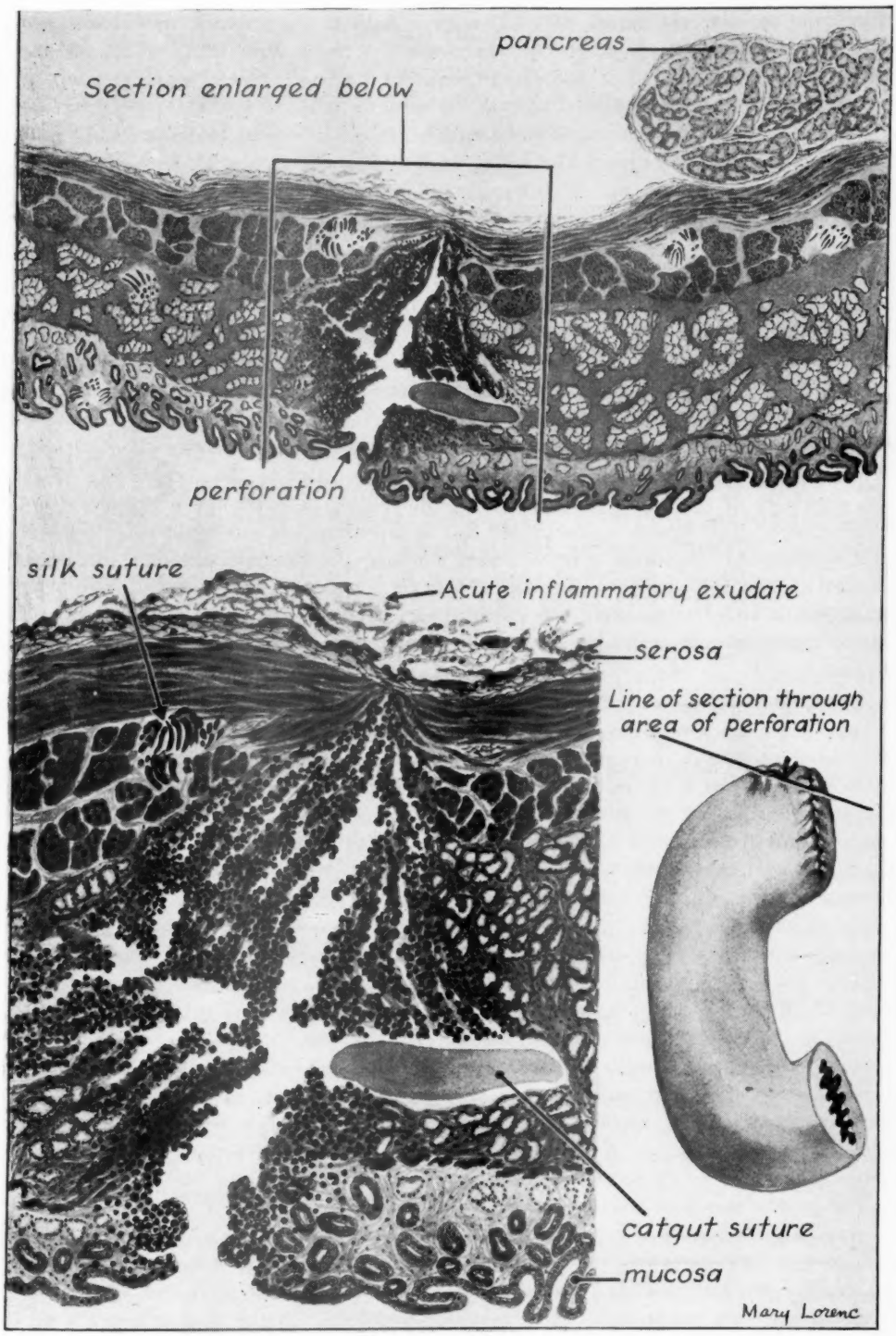

Fig. 1.—Duodenal stump and microscopic sections through area of perforation.

and there were many easily lysed adhesions between the small intestine, the omentum, the liver, and the anterior abdominal wall. The lower half of the stomach was absent and an anterior Pólya type gastrojejunostomy was present. There were many adhesions in the region of the gall bladder, which was dilated, and the duodenal stump. Approximately 1 cm. distal to the end of the duodenal stump on the anterior surface a plicated perforation was seen. The closure of the perforation was adequate and no intestinal contents could be forced through the area of perforation. The entire duodenum and proximal loop of jejunum up to the point of the jejunostomy was dilated and was bluish-black. The arrangement and color of the other organs of the abdominal cavity were normal.

Gastrointestinal Tract: The esophagus was normal. The distal half of the stomach, including the pylorus, was absent and an anterior antiperistaltic Pólya gastrojejunostomy was present. The stoma of both ostia easily admit the index finger. There was no excessive fibrosis or edema in the region of the ostia. The proximal loop of jejunum and the entire duodenum were dilated and dark red-blue. This color extended to the point of the gastrojejunostomy. No angulation or other mechanical reason for this could be found and no vascular occlusion of the regional blood vessels was present. The remainder of the gastrointestinal tract was normal in location and there were no gross lesions seen on the mucosal surface. On the anterior wall of the duodenum, 1 cm. distal to the end of the duodenum stump, a number of catgut sutures were found in the area in which the previous perforation had been closed. This closure was adequate and no intestinal contents could be forced through it. On opening the duodenum, stomach, and jejunum, the gastrojejunostomy was found to be patent and no evidence of ulceration or scarring could be found in the region of the anastomosis or near-by jejunum. No enlarged mesenteric lymph nodes were palpated. The colon contained formed, yellow-brown feces, and no evidence of gastrointestinal hemorrhage was found.

Duodenum: A section taken through the region of the perforation revealed the presence of a sinus tract coursing through the entire thickness of the wall. This placed the duodenal lumen and the serosa in communication with each other. This sinus tract contained purulent exudate and its walls were made up of hemorrhagic fibrous tissue that was infiltrated by a fairly small number of lymphocytes and polymorphonuclears. The fibrous reaction extended for a moderate distance into the duodenal wall on either side of the tract and the overlying submucosal and mucosal glands were atrophic in this region. Two sorts of suture material were seen in the vicinity of the sinus. Broad pink fibers were present in the fairly internal portions of the walls of the tract without inflammatory reaction. Deeper in its substance there was another type of suture material which was anisotropic and was composed of bundles of smaller fibers. The latter had the appearance of silk, and the former the appearance of catgut. Contiguous with the latter were large areas of foreign body giant-cell reaction, with numerous multinucleated giant cells and hemosiderin pigment. These areas were so large that they undoubtedly long antedate the surgical procedure performed the day before death. In a few instances the giant cells incorporate anisotropic foreign material. The process of chronic inflammation and necrosis extended for some distance into the serosal aspect of the duodenum. A small portion of the pancreas was included in the section. The duodenal wall in this region was entirely normal as was the subjacent glandbular parenchyma. A colony of bacterial growth was seen within the wall of the tracts.

Jejunum: Sections of jejunum were taken from the region of gastrojejunostomy stoma. Autolysis was very marked in the region of the mucosa and precise definition of this cellular characteristic was not possible. Nevertheless, there was extreme congestion of the veins of the submucosa with hemorrhagic extravasation and edema. There was a severe acute suppurative inflammatory reaction in the serosa and some infiltration of the muscularis and submucosa with polymorphonuclears as well. Some of the muscle nuclei were somewhat pyknotic and the muscle layers were disorganized, suggesting that the gut was on the way toward infarction.

CONCLUSIONS

This case presents a very unusual complication of surgical gastrojejunostomy. A 43-year-old white man underwent subtotal gastrectomy and anterior Pólya gastrojejunostomy for perforated gastric ulcer at another hospital, five and one-half months prior to his final illness. The anastomosis functioned well and was anatomically patent when he died. Two days before death, signs and symptoms of perforation of the upper gastrointestinal tract appeared suddenly and this was confirmed by laparotomy. The unusual feature was that the perforation took place not at this gastrojejunal anastomosis, but in the proximal portion of the duodenal stump at the site of the original closure. In this region the necrosis and acute inflammatory reaction of the perforation were distinguished from the foreign body giant-cell reaction in relation to the old suture material (silk). The proximal loop of jejunum was dilated, congested, and acutely inflamed. The most severe inflammatory reaction was in the peritoneum. Were it not for this, the changes in the jejunal wall would be those of early infarction. For this reason there are two alternative reconstructions of the sequence of events: (1) The proximal jejunal loop became dilated for some reason with infarction. The site of the duodenal closure with the foreign body reaction was a locus minoris resistentiae and gave way under the pressure. The peritonitis ensued. (2) The proximal stump in the region of the foreign body reaction perforated. The ensuing peritonitis resulted in ileus with subsequent involvement of the wall in the serosal inflammatory reaction. Functional obstruction of the proximal jejunal loop as a result of transient or persistent angulation sometimes complicates the anterior type of Pólya anastomosis and this may have been the initiating event. The regional blood vessels were dissected and no vascular occlusion was present.

There were clinical evidences of a blood transfusion reaction in the immediate postoperative period, including chills, fever, jaundice, and red urine. Although there were a few casts in the collecting tubules that resembled hemoglobin, the morphologic appearance of the kidney was not that of hemoglobinuria nephrosis. The visceral congestion was probably associated with the secondary shock.

SUMMARY

A case is reported in which there was perforation of the duodenal stump five and one-half months following subtotal gastrectomy. It is of interest because of the rarity of this complication so long after the original procedure. It is also important in calling this possibility to the attention of surgeons who might be faced with an acute abdomen in a patient several months after gastrectomy.

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PRIMARY OMENTAL CYST: A RARE CAUSE OF ACUTE ABDOMINAL SYMPTOMS

Case Report

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CYSTS of the omentum are rare. Those arising from sources outside the omentum—that is, omental cysts secondary to metastatic tumors, hydatid disease, or foreign bodies—are more common than primary cysts, which develop within the omentum itself. Only about one hundred primary omental cysts have been reported in the literature.[1-3]

The early symptoms and signs of a primary omental cyst usually result from a gradual enlargement of the cyst and are often thought to be caused by ascites, retroperitoneal tumors, or chronic gastrointestinal lesions. Rarely indeed does an omental cyst produce acute abdominal symptoms.

We are reporting the case of a 3-year-old boy with acute abdominal symptoms suggesting appendicitis with perforation, and on whom operation revealed an inflamed primary omental cyst.

CASE REPORT

A. R., a 3-year-old white boy, entered the Hospital of the University of Pennsylvania on Sept. 10, 1950. Two days before admisssion he first complained of mild generalized abdominal pain, but otherwise appeared well to his parents and received no treatment. On the following day he refused to eat and said that the abdominal pain was more severe. He was examined at home by his physician.

The rectal temperature was 102° F. but nothing was noted on physical examination to explain the fever. Abdominal and rectal examinations disclosed no abnormalities. On the following morning, forty hours after the onset of the abdominal pain, a rectal temperature of 103° F. and generalized abdominal tenderness were noted. The patient had not vomited and the bowels had moved normally. He was admitted to the hospital forty-eight hours after the onset of symptoms.

On first seeing the child in the hospital we were impressed by the healthy general appearance in spite of the fever and the signs of intraperitoneal inflammation. Temperature was 101.6° F., pulse rate was 134, and respirations 20. The abdomen was slightly and symmetrically distended. Peristalsis could be heard but the sounds were diminished in intensity and frequency. Palpation of the abdomen disclosed generalized guarding and tenderness that was equal in all quadrants. Rectal examination disclosed no masses. Physical examination showed no abnormalities outside of the abdomen.

The hemoglobin determination was 94 per cent and the leucocyte count 27,400. Examination showed no abnormalities outside of the abdomen.

Our preoperative diagnosis was acute appendicitis with perforation and peritonitis, although we recognized that the diagnosis was questionable because the history was not typical of appendicitis and because no localizing signs were present.

Operation was performed (by W. T. F.) under endotracheal anesthesia with cyclopropane and ether two hours after the patient's admission. The abdomen was opened through a right

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lower quadrant muscle-splitting incision that was enlarged by cutting across the posterior rectus sheath. The peritoneal cavity contained a large volume of cloudy fluid. The appendix appeared normal and was removed. A large, thin-walled cyst filled the anterior abdomen. Covering scattered areas of the cyst wall was a fibrinous exudate, which had produced a few loose adhesions to the small bowel. The cyst was inadvertently opened during its removal and was noted to contain about 500 c.c. of straw-colored fluid, a portion of which had clotted. The cyst lay within the greater omentum and extended from the transverse colon, to which it was loosely adherent, to the omental tip. It was removed in its entirety without opening the intestine, and the abdomen was closed without drainage.

After the operation, the patient was given 400,000 units of penicillin daily for 7 days by the parenteral route. Except for intermittent fever, which did not exceed one degree (F.), convalescence was uneventful. The wound healed by primary intention and the patient was discharged on Sept. 19, 1950. Examination one month after operation revealed no abnormalities.

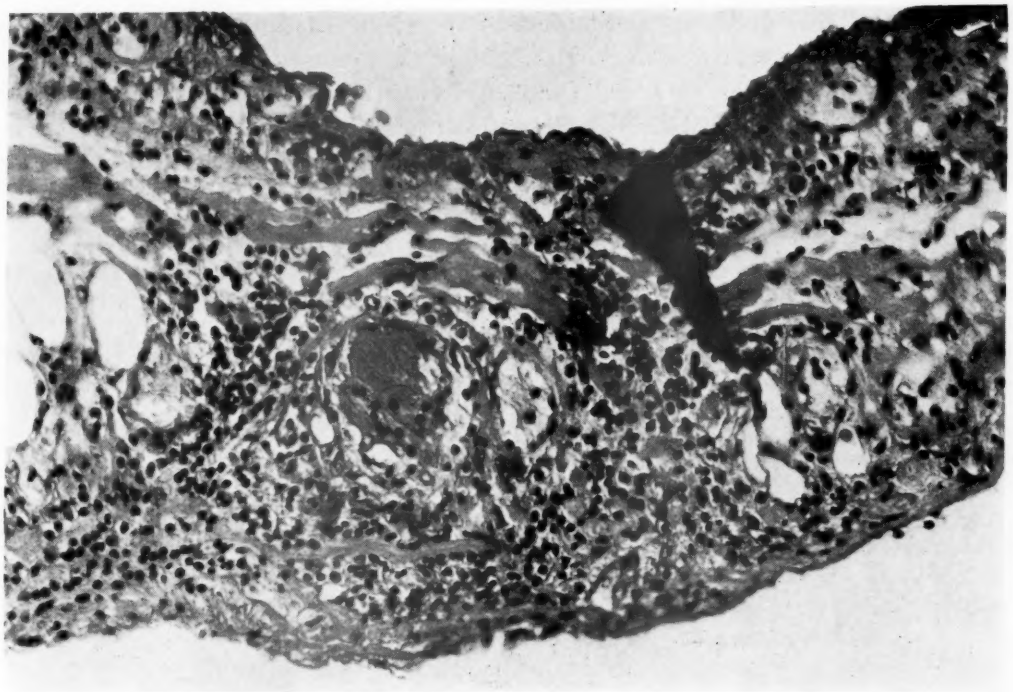

Fig. 1.—Cyst of omentum. Photomicrograph showing the inflamed cyst wall. On the upper surface a layer of low cuboidal cells may be seen lining this portion of the cyst.

Culture of Peritoneal Fluid.—No bacteria were observed on a stained smear of the peritoneal fluid, but hemolytic staphylococci grew on broth inoculated with the fluid.

Pathologic Examination (No. 82010).*—The specimen included a collapsed, thin-walled cyst of approximately grapefruit size and an appendix. The appendix was essentially normal both grossly and microscopically. On microscopic examination the cyst was seen to be lined largely by a layer of fibrinopurulent exudate, although patches of a single layer of low cuboidal cells (presumably mesothelial) were preserved in places. The thin, fibrous wall of the cyst and the surrounding omental adipose tissue showed intense acute inflammatory changes. Fig. 1 shows the cyst, which was diagnosed as a cyst of omentum (with acute inflammation).

*By Dr. Paul J. Cherney.

DISCUSSION

The pathogenesis of primary omental cysts is disputed. Although this case adds little to the knowledge of the origin of these cysts, it is unusual in the degree of inflammation involved. It is possible that the staphylococci cultured from the peritoneal fluid were contaminants and that the inflammatory changes noted in the cyst wall on microscopic examination were caused by exudation of lymph rather than by pyogenic bacteria. The patient's clinical course, however, suggests that infection in the cyst initiated the acute symptoms, in spite of the fact that the portal of entry for the organisms is obscure. The early development of high fever, the abdominal tenderness, and the high leucocyte count all indicate infection.

Few of the omental cysts reported in the literature have produced acute abdominal symptoms. Torsion of the cyst or pressure of the cyst on adjacent viscera have produced abdominal crises in a few instances. Eichwald[4] reported an omental cyst in a 3-week-old infant that caused death by obstructing the small intestine. Beahrs and Dockerty[3] reported a case similar to ours, in which the preoperative diagnosis was also appendicitis with perforation. In their case, however, hemorrhage was found in the cyst wall and no bacteria were demonstrated.

SUMMARY

An omental cyst in a 3-year-old boy produced acute abdominal symptoms suggesting a diagnosis of appendicitis with perforation. Culture of the peritoneal fluid and microscopic examination of the cyst wall suggested that the development of infection within the cyst initiated the acute symptoms.

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ENDOANEURYSMORRHAPHY FOR SPONTANEOUS INNOMINATE ARTERY ANEURYSM

Report of a Case With Cure and an Important Diagnostic Complication

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ALTHOUGH proximal ligation has been the surgical procedure most frequently employed for aneurysm of the innominate artery, the ideal treatment is generally considered to be proximal and distal ligation with excision of the sac where possible.[1-5] No instance of a deliberate endoaneurysmorrhaphy for innominate artery aneurysm is recorded despite the fact that this procedure permits preservation of arterial flow. In the present case, "restorative" endoaneurysmorrhaphy[6] appeared to be the procedure of choice and was carried out without special difficulty. The aneurysm was satisfactorily obliterated as shown by angiocardiography and the patient is well sixteen months postoperatively.

During evaluation of the lesion, catheter arteriography resulted in a severe right brachial plexus palsy. Since this occurred because of an avoidable technical error in a valuable and increasingly popular procedure, the incident is an important one. No similar accident has been found recorded in the literature.

CASE REPORT

M. M., a 47-year-old white man, a construction worker, was transferred to the Marine Hospital in Baltimore from the Marine Hospital in Kirkwood, Mo., on Sept. 3, 1949, with a provisional diagnosis of aneurysm of the right carotid artery due to syphilis. In 1924 the patient had a penile lesion but received no antisyphilitic treatment. Three months before admission he began to experience pain in the low anterior neck on swallowing and tenderness on the right side of the neck extending upward from the sternum just anterior to the sternocleidomastoid muscle. A slight swelling was noted in the area of tenderness. On admission to the Kirkwood Marine Hospital the serologic test for syphilis was positive. After five daily injections of bismuth, he was given a fourteen-day course of penicillin, during which the symptoms diminished markedly. He was referred to this hospital for definitive treatment of the cervical mass.

At the time of admission there was no cervical tenderness or pain on swallowing. There was, however, slight exertional dyspnea and a gagging sensation with coughing. No history of trauma could be elicited. There had been no recent weight loss, anorexia, malaise, or fever. The past history and the system review were essentially noncontributory.

Physical Examination.—The patient was a well-developed and well-nourished 47-year-old man who did not appear ill. He was well oriented, intelligent, and cooperative. Height was 5 feet 8½ inches, weight 183 pounds, temperature 98.6° F., pulse 90, respirations 20. The pupils were round, regular, and equal, and reacted to light and accommodation. The supraclavicular area on the right was full and a nontender pulsating mass could

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be felt under the clavicular attachment of the sternocleidomastoid muscle. The first and second heart sounds were palpable over the mass and a systolic murmur was audible on auscultation. No tracheal tug was felt. The chest was symmetrical and the lungs were clear to palpation and auscultation. Percussion revealed diminished resonance beneath the medial portion of the clavicle on the right. The heart was unenlarged to percussion, the rhythm and rate were normal, and there was no murmur. The aortic second sound was louder than the pulmonic second sound. Blood pressure in the right arm was 144 systolic and 104 diastolic. In the left arm it was 172 systolic and 106 diastolic. The right radial pulse was weaker than the left. The remainder of the examination was unremarkable.

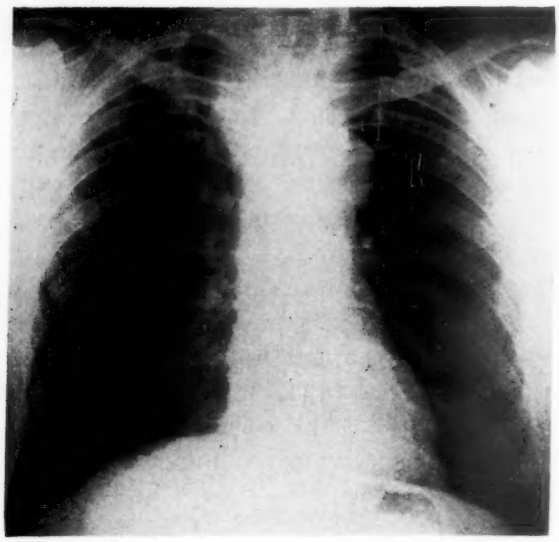
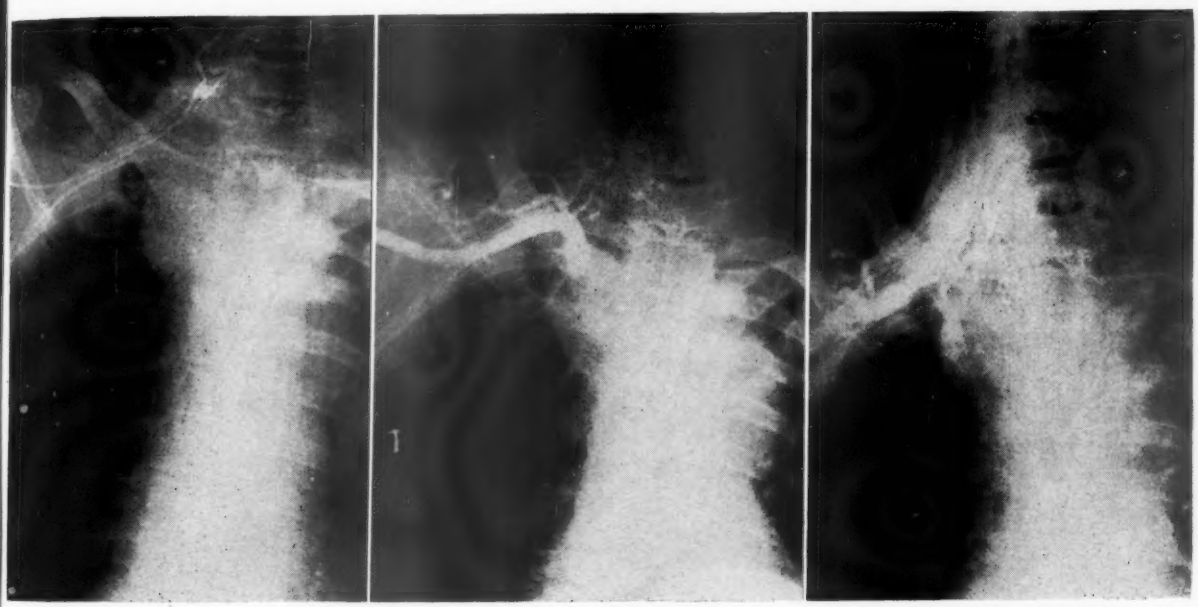


Fig. 1.—Roentgenogram of chest showing a dense mass in the region of the innominate artery. This measured 6.5 cm. in transverse diameter. It is not possible to determine from this film whether the aorta is involved.

Laboratory Data.—A Kahn test was 4 plus, a quantitative Kahn test was 8 units, and a Kolmer test was positive. The spinal fluid was clear, with a total protein of 45 mg. per cent and one lymphocyte per cubic millimeter. The spinal fluid Kolmer was 200000 and the colloidal gold test 0000000000. The white blood count was 8,750 with a normal differential, and the hemoglobin was 13 Gm. The urine was negative on admission except for 20 mg. per cent albumin and was subsequently entirely negative. The blood urea nitrogen was 16 mg. per cent, fasting blood sugar 79 mg. per cent, cholesterol 210 mg. per cent, total protein 7.8 Gm. with an albumin-globulin ratio of 1.6. A phenolsulfonphthalein test showed 40 per cent excretion in fifteen minutes and 85 per cent in two hours. The findings of an intravenous pyelogram were normal. The electrocardiogram, including six precordial leads, showed findings within normal limits. A phonocardiogram failed to reveal a diastolic murmur. The venous pressure was 11 cm. of saline and the circulation time, Decholin arm-to-tongue, seventeen seconds.

Multiple roentgenograms of the thorax showed an area of increased density 6.5 cm. in transverse diameter in the region of the innominate artery, best seen in the postero-anterior projection (Fig. 1). The trachea was deviated to the left. A roentgenogram made during a swallow of barium sulfate showed the esophagus displaced posteriorly and to the left at the level of the aortic arch. The aortic arch appeared somewhat dilated. No evidence of bony erosion was seen in any of the films. On fluoroscopy the mass was thought to pulsate and to be continuous with a dilated aortic arch. A retrograde arteriogram made by inserting a catheter through a needle into the right axillary artery showed

the subclavian artery and its branches to be normal. The distal portion of the innominate artery was visualized. It was markedly displaced to the right. The first portion of the subclavian artery was sharply angulated (Fig. 2, *B*). Direct right subclavian artery pressure tracings showed a blood pressure of 150 systolic and 85 diastolic. The pulse wave had an essentially normal contour. An angiocardiogram showed dense opacification of the mass. It was ovoid with a narrow base overlying the proximal innominate artery. It extended upward as far as the top of the first rib and clearly overlay the distal innominate artery and the proximal right subclavian artery. No vessels were seen leaving it, and the ascending aorta, aortic arch, and descending aorta appeared normal (Fig. 3, *A*). A roentgenologic diagnosis of saccular aneurysm of the innominate artery was made.



A. *B.* *C.*

Fig. 2.—*A*, The axillary artery catheter has entered a small branch of the second portion of the subclavian artery. *B*, The catheter has been withdrawn 2 cm. into the subclavian artery. It could not be made to pass the sharply angulated segment behind the clavicle. The contrast medium fails to fill the innominate artery or the aneurysm. *C*, An injection of Diodrast has been made with a catheter tip in a small branch, possibly that seen in *A*. The pressure of injection has resulted in extensive extravasation of Diodrast (and blood) into the tissue planes of the right neck. A brachial plexus palsy ensued. In addition to the extravasations, the free distal portion of the innominate artery is partially visualized.

Hospital Course.—The retrograde arteriogram was carried out on the twentieth hospital day under local anesthesia after completion of the initial studies. A 13 gauge hypodermic needle was inserted into the right axillary artery and through it was passed a polyethylene catheter.* The catheter was filled with a dilute solution of heparin in isotonic saline, passed for a distance of about 22 cm., and the needle withdrawn. Attempts to pass it beyond this point were unsuccessful. The arterial pulse was recorded using a Sanborn electromanometer and a positioning roentgenogram was taken during the injection of 1 c.c. of 70 per cent Diodrast. The catheter was seen to be in the mouth of a small artery (Fig. 2, *A*) and was consequently withdrawn 2 cm., after which blood could be freely withdrawn. After a suitable interval five pictures were taken in rapid succession during the injection of 30 c.c. of 70 per cent Diodrast in about 10 seconds. These pictures showed excellent opacification of the subclavian artery but failed to delimit the aneurysm (Fig. 2, *B*). The catheter was advanced about 2 cm. Blood could still be withdrawn

*Inside diameter 0.047 inch. Outside diameter 0.067 inch. Clay-Adams Co., Inc., New York, N. Y.

freely but a positioning film was not taken. A second injection of 30 c.c. of 70 per cent Diodrast in about 8 seconds was made. The patient immediately experienced considerable pain in the lateral and posterior aspects of the right neck. The films showed multiple areas of extravasated Diodrast along the tissue planes extending from the midcervical region almost to the axilla. The distal portion of the innominate artery was outlined but the aneurysm was not filled (Fig. 2, *C*). Following the injection, it was noted that the patient was unable to move his hand and forearm but there was no diminution in the radial pulse. The paralysis at this time was thought to be due primarily to infiltration of the brachial plexus with Xylocaine hydrochloride at the time of the arterial puncture. The following morning, however, the patient exhibited a severe brachial plexus palsy with almost complete paralysis of the biceps, triceps, and deltoid muscles, together with weakness of the forearm and hand muscles. Continuous hot wet dressings were applied to the neck and physiotherapy in the form of slow sinusoidal current was administered to the involved muscles. There was slight return of function in three to four days. An airplane splint was employed to maintain proper position.

A. *B.*

Fig. 3.—*A*, Preoperative angiocardiogram, posteroanterior projection. The mass seen in the plain film is densely opacified. The aorta is not dilated, and there is a short section of apparently uninvolved innominate artery. *B*, Angiocardiogram about ten weeks postoperatively, right posterior oblique projection. The aorta is normal in contour. The midportion of the innominate artery is only slightly larger than normal.

On the twenty-fourth hospital day right carotid compression for ten seconds resulted in syncope. This was repeated several weeks later and prolonged compression caused no syncope or electrocardiographic change. On the thirty-seventh hospital day an uneventful angiocardiogram was carried out and the probable diagnosis of saccular aneurysm of the innominate artery established.

On the fortieth day the chest was explored under endotracheal ether anesthesia.* Exposure of the anterior superior mediastinum and neck was secured by resecting the

*The senior author effected the exposure after which the aneurysmorrhaphy was simply executed by the junior author.

medial half of the right clavicle, performing an upper median sternotomy, dividing the first three ribs anterolaterally, and turning back the right costosternal window thus formed. A large saccular aneurysm of the innominate artery was found (Fig. 4). This was freed up and the proximal innominate artery, right carotid artery, and right subclavian artery mobilized. The free proximal portion of the innominate artery was very short and markedly thickened by adventitial scarring associated with the overlapping aneurysmal sac. Blood flow could not be occluded with a tape, so a Blalock curved coarctation clamp was utilized. Heavy serrefine clamps were found to be satisfactory for occlusion of the subclavian and right common carotid arteries. With control of the circulation, the aneurysmal sac was opened and pared back. The arterial lining that could be seen beyond the aneurysm appeared fairly normal. It was closed with a mixture of 0000 silk on fine cutting needles and 00000 silk on large atraumatic arterial needles. Small atraumatic arterial needles were found to be too weak to sew the greatly thickened sac neck. Simple interrupted sutures passing from side to side were employed and the loose proximal sac wall was plicated over the repair. The entire innominate artery was then wrapped with fibroplastic polyethylene film.* Occlusion time for the innominate artery was approximately 60 minutes. No anticoagulants were used. A Penrose drain was left in place. The microscopic diagnosis of the aneurysmal wall was "innominate arteritis consistent with syphilitic origin."

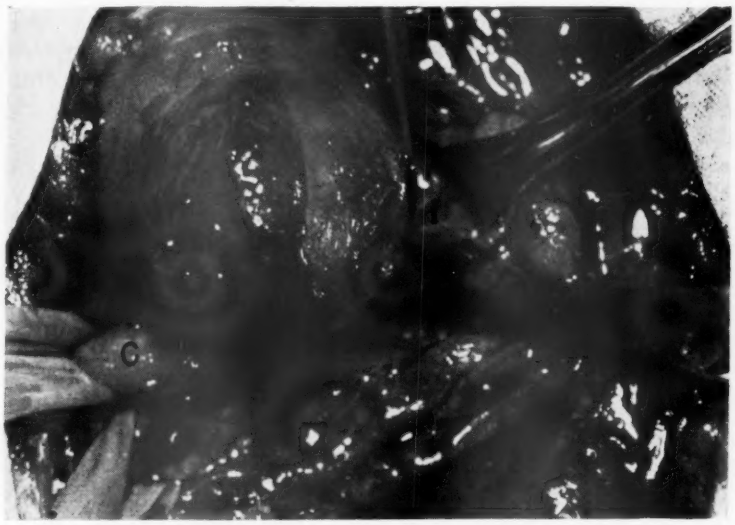


Fig. 4.—Operative photograph showing the exposed aneurysm, proximal innominate artery (*I*), common carotid artery (*C*), and subclavian artery (*S*). A rubber drain or narrow tape has been passed around each. It was not possible to control the innominate artery with a tape, but a curved coarctation clamp proved very satisfactory.

The postoperative course was smooth except for moderate fever during the first three days. There was no evidence of cerebral damage and the right radial pulse remained palpable. The right diaphragm was elevated and persisted in this position, suggesting some phrenic nerve damage. The drain was removed on the third postoperative day and ambulation and physiotherapy were resumed ten days postoperatively. Penicillin, 1,200,000 units daily, was given for sixteen days. At the time of discharge on the sixty-sixth hospital day there was moderate and increasing improvement in the function of the muscles of the right upper extremity. Physiotherapy was continued after discharge, at Kirkwood, Mo.

*Type NV-7-14 solvent-cast Polythene with dicetyl phosphate. DuPont de Nemours and Co., Cellophane Division, Wilmington, Del.

The patient was readmitted Jan. 16, 1950, for follow-up studies. Since discharge there had been continuing improvement in the strength of the right arm, forearm, and hand, with weakness limited mainly to elbow flexion and shoulder abduction. There had been no recurrence of preoperative symptoms and very little limitation of activity although the patient had not returned to work. Physical examination revealed the incision to be well healed and nontender. The right shoulder was partially fixed and there was marked deltoid, biceps, and triceps atrophy. Forearm extension was good but flexion was poor, the patient being barely able to initiate motion against gravity. The wrist was strong, the flexors overbalancing the extensors somewhat. There was no loss of intrinsic finger motions. The neck was supple and there was no limitation of motion of the right chest. The lungs were clear except for a slight diminution in breath sounds, without a percussion change, just to the right of the upper sternum. The heart was unenlarged and not remarkable except for a Grade I apical systolic murmur. A_2 was greater than P_2. The remainder of the examination results were within normal limits. Pertinent laboratory data included a 2 plus Kahn test, and a 4 plus quantitative Kahn test. A roentgenogram of the chest revealed a minimal increase in density in the right upper lung field. There was no mediastinal enlargement as had been present preoperatively. On the second hospital day an angiocardiogram was carried out without difficulty. This showed a wide, quite regular innominate artery without evidence of aneurysm or narrowing (Fig. 3, *B*). The patient was instructed in shoulder exercises and discharged on Jan. 19, 1950, fit for light work.

The patient was again seen on June 17, 1950. Since discharge he had been working steadily as a drag line operator and had noted progressive, although not complete, return of strength to the right arm and hand. There had been no dysphagia, pain, cardiovascular or respiratory symptoms. Examination revealed only moderate atrophy of the right arm muscles, biceps atrophy being most marked. There was still some shoulder fixation. All muscles were strong, but weaker than those of the left upper extremity. The neck was supple and the chest symmetrical. Lungs were entirely clear, and the heart as at the previous examination. Findings of an electrocardiogram were normal. The Kahn test was doubtful but the Kolmer test was positive. A roentgenogram of the chest showed the lung fields to be clear. There was no increase in the mediastinal shadow. The patient was discharged to be followed for his syphilis at the Kirkwood Marine Hospital.

A follow-up by letter in February, 1951, revealed the patient working regularly and with no symptomatic complaints.

DISCUSSION

Innominate artery aneurysms comprise about 3 per cent of the total and are most commonly spontaneous (syphilitic) in origin.[2] These, unfortunately, generally involve the aortic wall, while aneurysms limited to the innominate artery and presently amenable to surgery are infrequent. Matas[6] recorded 10 pure innominate lesions among 1,147 cases of aneurysm.

Diagnosis in previous surgical cases has been made without the use of contrast aortography. More precise evaluation is now possible with the use of angiocardiography,[8] retrograde arteriography,[9] or catheter arteriography.[10, 11] The simplest of these is angiocardiography. It was diagnostic in the present case (Fig. 3, *A*) and also in a case of a fusiform aneurysm not coming to surgery reported by Maddox.[7] An inoperable aneurysm of the innominate artery has been diagnosed also by percutaneous femoral artery catheter arteriography.[11]

Prior to angiocardiography, a catheter was passed via the right axillary artery but the aneurysm could not be outlined because of angulation of the subclavian artery. Although a portion of the innominate artery was opacified,

it was at the cost of a brachial plexus palsy. This accident demonstrates that the pressure from hand evacuation of a small hypodermic syringe is sufficient to cause arterial rupture if that pressure is delivered by a catheter into a partly occluded artery. Persons performing arterial catheterizations for roentgenographic purposes should therefore probably observe the following precautions: (1) Obtain a check film for position of the catheter tip immediately prior to injection. (2) Withhold injection if the tip is not in a large artery or if blood fails to reflux freely into the catheter.

Sympathectomy has recently been advocated as a preliminary to definitive surgery for aneurysms of large arteries.[4, 12] Since there are no recorded cases of gangrene of the arm following ligation of the innominate artery,[3] this would appear to be ordinarily unnecessary and was not employed in the present case. Carotid compression has almost universally been recommended as a necessary preparation for innominate surgery. This may be carried out digitally or when necessary by application of metal bands. In our case the first attempt at compression resulted in immediate but brief syncope while subsequent prolonged compression had no demonstrable effect. Operative occlusion of the right common carotid for one hour was later done without complication.

Wide exposure was achieved by an anterior extrapleural approach, combining upper median sternotomy with resection of a portion of the clavicle as advocated by several authors and recently discussed fully by Schumacker.[13] The degree of exposure achieved is seen in Fig. 4.

TABLE I. RESULTS OF OPERATIVE PROCEDURES FOR ANEURYSMS OF THE INNOMINATE ARTERY*

OPERATION	NUMBER	IMPROVED AND CURED	DEATHS	OTHER
Attempted ligation	5		5	
Proximal ligation alone or with one distal vessel	36	17	15	4
Complete proximal and distal ligation	7	6	1	
Reconstructive procedures	3	3		
Totals	51	26	21	4

*Thirty-eight operations on 36 patients reported by Schumacker,[4] 12 additional cases reported by Gordon-Taylor,[5] plus the present case.

Excluding wiring, distal ligation alone, and production of a distal arteriovenous fistula, fifty-one direct operative attempts to treat aneurysms of the innominate artery have been carried out (Table I). The various cases have been comprehensively reviewed.[1, 5] Proximal ligation, occasionally combined with ligation of one distal vessel, has been reported in thirty-six instances with fifteen deaths and seventeen patients cured or improved. Isolation of the aneurysm by ligation of innominate, common carotid, and the first portion of the subclavian arteries has been effected only seven times with six satisfactory results and one death. In only one of these cases was complete sac excision carried out, while two had partial excision. Prior to the present case, there were only two instances of innominate artery reconstruction. In one, a small fusiform aneurysm was reduced to normal caliber by wrapping with fascia lata,[14] and

in the second, a rent in the artery leading to a false traumatic aneurysm was sutured.[15] After ligation of the proximal innominate artery, Flint,[16] to control a hemorrhage, partially obliterated the sac from within. It has not been possible to find any reference to even an attempted endoaneurysmorrhaphy and there are several authors who state that this procedure is not suited to innominate artery aneurysm.[2-5] In 260 operations for aneurysms, Matas carried out thirty "restorative" or "reconstructive" endoaneurysmorrhaphies and the largest artery involved was the axillary.[6]

The desirability of preserving arterial flow through the common carotid and subclavian arteries is readily apparent. In the present case, excision with use of a viable homologous arterial graft was planned, if feasible. Since the aneurysmal neck was narrow and the remainder of the artery was not grossly diseased, endoaneurysmorrhaphy seemed the procedure of choice. Adequate exposure and complete control of the proximal innominate, subclavian, and common carotid arteries made the operation technically fairly simple. The redundant proximal sac wall provided ample tissue for reinforcing the closure of the neck and the whole was easily wrapped in fibroplastic Polythene to promote fibrosis and prevent recurrence.[17] The postoperative arteriogram demonstrates that the innominate artery is without residual aneurysm and only slightly dilated. Naturally the end result must wait the test of time, but the absence of aortic dilatation and valvular disease, plus the initial cure, suggest a good prognosis. Endoaneurysmorrhaphy would appear to have less danger of secondary complication than triple ligation alone, and to be much less formidable than ligation plus excision. It is hard to believe that other saccular innominate artery aneurysms will not at least occasionally be amenable to reconstructive surgery. The technical advances that have made the region of the great vessels "now territory into which even the novice may penetrate with certainty and safety"[5] would appear to refute the general pessimism in regard to reconstructive procedures for aneurysm of the innominate artery.

SUMMARY

A case of classical saccular aneurysm of the innominate artery repaired surgically by endoaneurysmorrhaphy with restitution of blood flow is reported. The operative results were demonstrated by angiocardiography and the patient was clinically well sixteen months postoperatively. This appears to be the only recorded instance where an endoaneurysmorrhaphy was employed in treating an aneurysm of the innominate artery. The case also presents a serious complication of catheter arteriography: arterial rupture with widespread extravasation of Diodrast and consequent brachial plexus palsy. The cause of this complication and means of preventing similar accidents are discussed.

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PHLEGMASIA CERULEA DOLENS—SUCCESSFUL TREATMENT BY VENA CAVA LIGATION

Case Report

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PHLEGMASIA cerulea dolens is a form of thrombophlebitis of the lower extremities in which there is fulminating venous thrombosis accompanied by marked reflex arterial spasm. Approximately 50 per cent of the patients progress to gangrene of the involved extremity. Because of the severe arteriospasm, the entity is frequently mistaken for arterial embolism from which it derives one of its many designations, i.e., pseudoembolic phlebitis.

Clinically the disease differs from the usual type of thrombophlebitis (phlegmasia alba dolens) in that the onset is more sudden and the symptoms are more severe. In addition there are the distinguishing features of a violaceous discoloration of the skin of the affected extremity, with temperature and sensory alterations; and the signs of vascular impairment, i.e., diminished or absent arterial pulsations of the involved extremities (due to vasospasm); and the symptoms and findings of varying degrees of shock.

Phlegmasia cerulea dolens may exist more often than the literature suggests, because of the concomitant arterial spasm in most cases of thrombophlebitis and phlebothrombosis. Vena cava ligation, with its increasing popularity,[3, 8] may have been employed for phlegmasia cerulea dolens when the surgeon believed the condition to be one of ordinary thrombophlebitis or phlebothrombosis.

Phlegmasia cerulae dolens was first described in 1929 by Trémolières and Veran,[7] and attention was again directed to it in 1938 by Gregoire.[2] Only three cases had appeared in the American literature until DeBakey and Ochsner[1] reported two cases in 1949.

The purpose of this report is to add another case of phlegmasia cerulea dolens to the small number (fifty-nine) that have been reported in the literature and to describe the effect of vena cava ligation. Oaks and Hawthorne[4] in 1948, and Young and Derbyshire[9] in 1950 reported recovery as a result of this operation. Sympathectomy was not performed in either case.

CASE REPORT

R. R., a 27-year-old white man, was admitted to the Orthopedic Section of Kennedy Hospital on Oct. 6, 1950, because of a fractured pelvis which he had sustained three weeks previously in a fall from a tree. He had previously been treated with bilateral leg traction at another hospital.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Received for publication, March 20, 1951.

Physical Examination.—Temperature, pulse and respiration were normal. Examination was essentially negative. A short spica cast had been applied for easy transportation. X-rays of the pelvis revealed healing fractures of the superior and inferior rami of the right pubis with good alignment of the fragments. Results of routine laboratory studies were normal.

Hospital Course.—Bed rest in a pelvic sling was the treatment employed, and the patient progressed normally until 12:30 A.M. on Oct. 17, 1949, when he was awakened by the sudden onset of a severe aching pain in the left inguinal region which later extended into the medial aspect of the left thigh. This was soon followed by severe cramping in the left calf and swelling of the left thigh and leg. These symptoms grew in severity and the patient became increasingly restless and apprehensive.

Eleven hours after the onset, the patient was exceedingly apprehensive and acutely ill, presenting the picture of incipient shock. The face was ashen gray and wet with perspiration, the skin cold and clammy. He complained of severe pain in the left leg, but there had been no chest pain, dyspnea, or hemoptysis. The temperature was 98.6° F. The pulse rate was 130 to 140. The character of the pulse was weak and irregular. The left lower extremity was cold, wet, diffusely edematous, and reddish blue in color. The left dorsalis pedis artery pulsation was absent, the left posterior tibial, the left popliteal, and the left femoral pulsations were markedly diminished as compared to normal pulsations in the opposite extremity. Calf tenderness and tenderness over the course of the left femoral vein were present. There was a positive Homans' sign on the left.

During the examination the patient became rapidly worse, the degree of shock becoming more profound. The left posterior tibial artery pulsation disappeared and the left femoral pulsation became barely palpable. The blood pressure was 60/40 and a diagnosis of phlegmasia cerulea dolens was entertained. The possibility of extending thrombosis and pulmonary embolism prompted a consideration of vena cava ligation. The shock was so pronounced that the patient was transported to the operating room in his bed.

Spinal anesthesia was induced, the vena cava was exposed retroperitoneally, ligated doubly with No. 4 silk ligatures, and divided. A clot was noted within the lumen of the vena cava and was removed. This later proved to be bacteriologically sterile and not remarkable from a pathologic standpoint. Immediately after the vena cava was ligated the general condition began to improve. The anxiety and apprehension disappeared and the pulse and blood pressure improved considerably. The cyanosis disappeared rapidly. During and immediately after the procedure transfusions of 500 c.c. of plasma and blood were given. Before the patient was returned to the ward both feet became warm, the left posterior tibial and dorsalis pedis pulsations reappeared, and the volume of the left femoral pulsation approached normal. The blood pressure improved during operation, but remained around 100 mm. mercury systolic until several hours postoperatively, when it gradually returned to a normal level.

There could be no possible cutting of lumbar sympathetic nerves on the involved side.

The patient was mildly disoriented for several hours and vomited occasionally during the early postoperative days. Slight edema of both legs was present, and the feet were intermittently warm and dry or cold and wet, but never appeared cyanotic.

Postoperative treatment consisted of pressure bandages, papaverine, whiskey, and penicillin in addition to continued treatment of the fractured pelvis. Lumbar sympathetic blocks were carried out because signs indicated vasospasm, and, although the results were excellent objectively according to oscillometric, skin temperature, and skin resistance determinations, they were poor subjectively, inasmuch as cold, wet feet did not inconvenience the patient as much as the pain from the sympathetic blocks. Dryness of the skin was noticed for short periods of time, while warmth remained for longer periods. The patient became ambulatory without crutches on Nov. 16, 1949.

The fractured pelvis healed normally and the patient was discharged from the hospital on Nov. 21, 1949, approximately five weeks after the ligation.

At the follow-up examination Feb. 20, 1950, the patient complained of swelling of the feet after standing or walking longer than four hours, but this was relieved by resting for a few minutes. He stated that the edema gradually diminished so that since January, 1950, elastic bandages were no longer necessary. There were no other complaints.

Examination at this time revealed no edema of the lower extremities. They were of normal color and the peripheral arterial pulsations were present and equal bilaterally. The feet were intermittently cold and wet, which suggested a continued unstable vasomotor mechanism.

On Oct. 12, 1950, one year after operation, the patient was seen in follow-up examination. He complained of mild cramping in the calves after retiring but was otherwise asymptomatic and worked from 8 to 10 hours a day. Examination of the lower extremities revealed no edema or discoloration, and all the peripheral arterial pulsations were normal except for the left dorsalis pedis which was diminished. Oscillometric and skin temperature determinations revealed no abnormal deviations.

Comment.—The inferior vena cava was ligated in this case primarily to prevent pulmonary embolism, inasmuch as clinically the thrombus had been observed to extend well into the left common iliac vein and to be devoid of inflammatory element. Operation revealed upward progression of the thrombus as it was found lying free in the lumen of the inferior vena cava.

The excellent physiologic response elicited almost immediately after ligating the vena cava came somewhat as a surprise to us, for, at the time, we were not aware that this procedure had been employed previously in the treatment of this disease.

It is difficult to explain why, after ligation of the inferior vena cava, there was immediate improvement in the patient's general condition with disappearance of shock and return of arterial pulsations in the affected extremity. However, we have observed effects akin to these many times after ligation of the superficial and common femoral veins in the treatment of phlebothrombosis and thrombophlebitis of the deep veins of the lower extremities. Ray and Burch[5] believe that vena cava ligation usually induces diminution of arterial pulsations in the affected extremity.

It may be contended that the arterial responses are due to spinal anesthesia. This is doubtful, because the spinal anesthetic was of a degree to cause relaxation of the abdominal wall musculature, and had been in effect for more than twenty minutes, but no vascular effects were noted until the vena cava was ligated.

In the previously reported cases, arterial pulsations reappeared before caval ligation, and sympathetic blocks were so intimately associated with the return of pulsation, that it is impossible to designate the improvement to the ligation alone.

Shafiroff[6] postulated that the beneficial effect may be due to slowing of the venous circulation in the lower extremities, which allows biochemical antibodies in increasing concentrations to act upon the disease process. On the other hand, the inference may be drawn that some unknown factor deleterious to the cardiovascular and/or nervous systems is partially prohibited from returning

to the systemic circulation and is more or less confined to the veins distal to the ligature. The existing confusion suggests the need for further investigative work in this field.

Although diminution in arteriospasm was achieved without sympathectomy or sympathetic blocks during the operation, it is felt that sympathectomy could profitably accompany ligation for right-sided lesions.

SUMMARY AND CONCLUSIONS

1. A case of phlegmasia cerulea dolens successfully treated by ligation of the inferior vena cava has been reported.

2. This case, along with two cases reported elsewhere, has demonstrated the favorable effect of the ligation without gangrene or other serious sequellae.

3. It is suggested that vena cava ligation may be the method of choice in the treatment of this disease. Sympathectomy or sympathetic blocking may be useful adjuncts.

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PULMONARY RESECTION FOR METASTATIC FIBROSARCOMA

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THE disclosure of a solitary metastatic lesion of the lung months or years following presumably complete removal of a primary extrapulmonary malignancy is by no means uncommon. While surgical resection of the affected lobe or lung constitutes a distinct gamble, it offers the patient his only chance to elude certain death. Alexander and Haight,[1] in 1947, published a collected series of twenty-four case reports in which both the primary and the metastatic pulmonary lesions had been removed. In this series, the longest interval between the removal of the primary lesion and the divulgence of a solitary pulmonary metastasis was thirteen years (case of Brezina and Lindskog). Alexander and Haight list three criteria for the removal of a presumed solitary pulmonary metastasis: 1. A thorough physical and x-ray examination shall have discovered no other metastases. 2. Reasonable assurance should be had that the primary growth has been completely removed. 3. The patient must be in sufficiently good general health to undergo pulmonary resection, and be able to spare a lobe or lung.

The following case report is submitted, in which a pulmonary metastatic lesion became manifest twenty-five years after removal of the primary growth.

CASE REPORT

Mrs. S. J., a 37-year-old white woman, enjoyed excellent health until January, 1950, when she first noted painful swelling of the terminal phalanges and increasing fatigue. Some time during the month of May she developed a slight but persistent hacking cough, unproductive of sputum and exaggerated by lying down. Concomitant with the appearance of the cough she experienced frequent bouts of pain and stiffness in the back and in the joints of all extremities. These bouts seemingly were precipitated by chilling, which of itself constituted a new symptom. She checked her afternoon temperature on several occasions and found it to be 100° F. Because of the aforementioned symptoms she finally sought medical advice in July.

Family History.—Father, age 83, was living and well; Mother, age 64, was living and well; one brother, age 35, was living and well. There was no family history of tuberculosis or malignancy.

Personal History.—The patient, para i, gravida i, had been married 13 years, and had a 4-year-old daughter who was living and well. Onset of menses had been at age 13. Menstrual periods were regular every 21 days with a 5 day flow which was not excessive. She ordinarily did her own housework without difficulty. She smoked 3 to 4 cigarettes a day.

According to the patient's statement, a below-the-knee amputation was done in 1925 because of an injury to the lower extremity. Upon interrogation of her mother, however, it was ascertained that the indication for amputation was a "tumor." The pathologist's report of the microscopic examination of the biopsy specimen was then secured. It was fibrosarcoma of fascia of the foot.

History by systems was negative except as indicated.

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Fig. 1.—Chest film demonstrating rounded shadow with smooth margin in the left cardiophrenic angle.

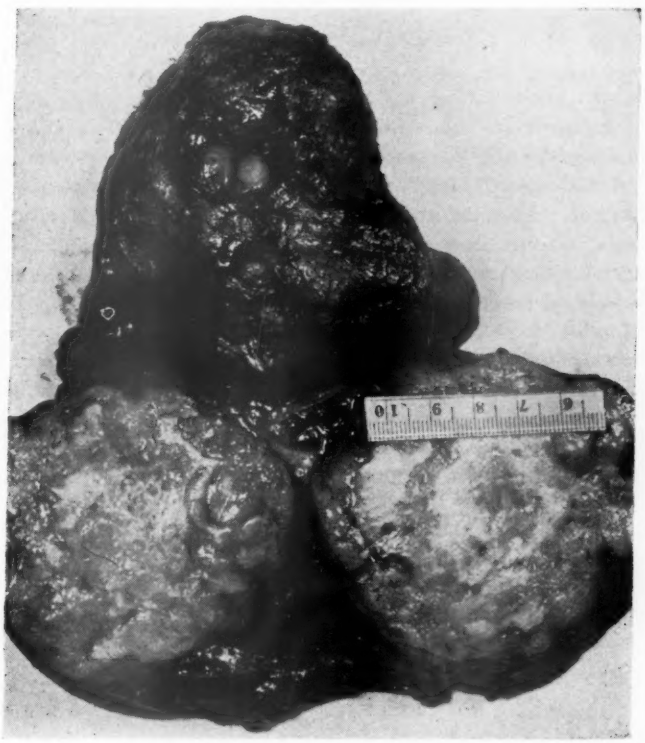

Fig. 2.—Resected lung showing large spherical tumor in the lower lobe. A smaller lesion is visible in the upper lobe.

Physical Examination.—Initial physical examination revealed an intelligent, alert 37-year-old white woman who did not appear acutely ill. Height was 5 feet, 4¾ inches, weight 119½ pounds, pulse 96, blood pressure 100/58, and temperature 100° F. It was noted that the left leg had been amputated about 4 inches below the knee. There was marked clubbing and red discoloration of the terminal phalanges of all fingers. Examination of the chest was entirely negative except for a few scattered râles in the left lateral base after coughing. The remainder of the physical examination was entirely negative.

X-ray studies included stereoscopic anterior posterior projection films of the chest, and intravenous and retrograde pyelography. The chest film demonstrated a rounded shadow with a smooth margin in the left cardiophrenic angle, its base resting on the left hemidiaphragm (Fig. 1). The greatest diameter of this mass was 7.5 cm. Another smaller opacity, with a less well-defined border, was also present in the upper third of the left lung field.

Laboratory Data.—Hemoglobin was 10.6 grams (69 per cent), red blood count 4,000,000, white blood count 11,400. Wassermann reaction was negative. Blood sedimentation was 37 mm. in 60 minutes. Sputum examination was negative for malignant cells and for tubercle bacilli. Urinalysis was negative for albumin, sugar, and cells. Specific gravity was 1.015.

Bronchoscopic examination revealed a normal tracheobronchial tree; and bronchial washings and smears were negative for malignant cells. Immediate exploratory thoracotomy was advised, but the patient demurred for a month, so that it was not until September that operative intervention was actually undertaken.

Operative Procedure.—The left pleural cavity was opened through a posterolateral incision removing a long segment of the sixth rib. A large spherical tumor mass occupied most of the lower lobe and was firmly attached to the dome of the left hemidiaphragm (Fig. 2). A smaller spherical mass was palpated in the upper lobe. The left lung, together with the hilar nodes, was removed, using individual dissection and ligation technique to deal with the pulmonary vessels and the left bronchus. It was necessary to remove that portion of the left hemidiaphragm to which the tumor was attached to effect complete removal.

Gross pathologic examination of the resected lung revealed a well-circumscribed, firm, white, nodular tumor in the lower lobe measuring 7 cm. in diameter. The tumor mass extended through to the pleura at the point of diaphragmatic attachment. The bronchi leading to the lower lobe were not involved, but were displaced around the periphery of the tumor. Another nodular tumor mass was demonstrated in the left upper lobe which measured 1.5 cm. in diameter. The microscopic diagnosis of sections stained with hematoxylin and eosin was fibrosarcoma, Grade III. The hilar lymph nodes appeared to be free from involvement.

The patient made a satisfactory recovery from the pulmonary resection but developed an acute intestinal obstruction six months later. Abdominal exploration revealed a solitary fibrosarcoma of the distal ileum as the cause of the obstruction. The tumor-bearing portion of the ileum was resected and end-to-end ileo-ileostomy performed. While convalescing from this operation she manifested signs of cerebral involvement and died on the twenty-first postoperative day, presumably from cerebral metastasis.

SUMMARY

A case is reported in which pulmonary metastasis became manifest twenty-five years after removal of a fibrosarcoma of the fascia of the foot.

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PARATHYROID CYST: AN UNUSUAL CERVICAL TUMOR

Report of Three Cases

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RARELY do cysts of the parathyroid gland attain such size as to deserve surgical attention. Some investigators[1, 2] have indicated, however, that cysts of microscopic and near microscopic size would be discovered in nearly every adult cadaver if serial sections were made of all four parathyroid glands. It is therefore surprising that the literature contains so very few instances of surgical removal of such cysts. Beginning in 1906, when Goris[3] described the surgical excision of a parathyroid cyst, only eight authentic cases have appeared in medical writing. The foreign literature[3-7] contains five cases. The American reports,[2, 8] both of which have appeared in the past five years, include three more examples.

Prior to January, 1950, the surgical pathology records at The Johns Hopkins Hospital contained no recognized case of a parathyroid cyst. During the ensuing nine months, however, a parathyroid cyst was removed from each of three patients. Inasmuch as cysts of the parathyroid gland heretofore have received scant consideration in the differential diagnosis of cervical enlargements, a report of these cases seems worth while.

REPORT OF CASES

Case 1 (J. H. H. 450528).—A 66-year-old white man was admitted to the surgical wards for thyroidectomy, having had symptoms and signs of hyperthyroidism for about two years. A lump was said to have been present in the left side of the neck for some eighteen years. He had been treated for seven months with propylthiouracil without interruption, with progressive remission of the hyperthyroidism. However, as the mass had not changed appreciably in size, thyroidectomy was advised. Lugol's solution was administered for ten days before operation.

On physical examination the mass in the left side of the neck was noted, and it was thought to arise in the left lobe of the thyroid. No bruit was heard. The right lobe was thought to be diffusely enlarged. The basal metabolism rate was plus 6.

At operation on Jan. 17, 1950, the left lobe of the thyroid was exposed first, and an adenoma the size of a chicken's egg was demonstrated at the left inferior pole of the thyroid. The right lobe was also inspected and found to be diffusely enlarged. A curious thin-walled cyst containing clear fluid was discovered, originating adjacent to the right inferior thyroid artery. It descended into the superior mediastinum and was in contact with the pleura. The nature of the cyst was not suspected. It was removed intact and measured 4 by 2 cm. A subtotal thyroidectomy was performed, including the adenoma on the left. The patient made an uneventful recovery.

The specimen of thyroid revealed typical hyperplasia. The cyst wall consisted of smooth, translucent tissue. A section was taken at random from this. Parathyroid tissue was found embedded in the wall (Fig. 1), the cells of which were in places arranged in an

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acinar pattern, with occasional central colloid droplets. Cuboidal epithelium lined the major cyst. Many small ramifications of the cyst projected into its wall, and these were lined by the same epithelium.

CASE 2 (J. H. H. 530623).—A 49-year-old housewife was admitted to the hospital for removal of a "goiter." A lump in the right side of the neck had been noted one year previously. Although there were times when it would rather rapidly increase or decrease in size, on the whole it progressively enlarged. The mass was asymptomatic save for occasional minor interference with breathing when the patient lay flat on her back. There were no factors suggesting either hyperthyroidism or hyperparathyroidism.

Significant physical findings were limited to the neck, where a smooth, soft mass was present in the region of the right lobe of the thyroid and extended inferiorly toward the sternal notch. It was estimated to be about 5 by 4 by 4 cm. in size. Routine laboratory studies were negative.

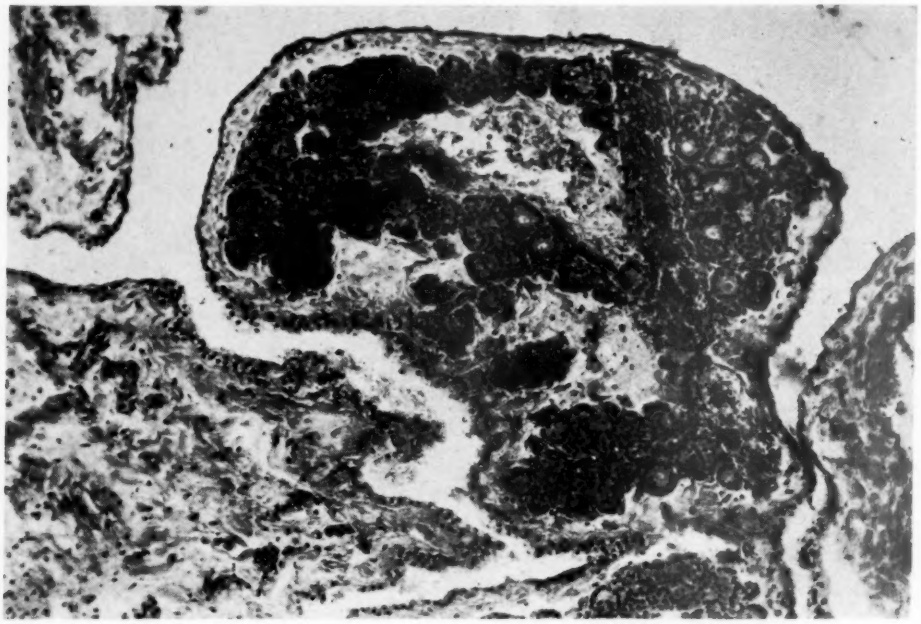

Fig. 1 (Case 1).—Parathyroid tissue projecting into the parathyroid cyst. This shows the cuboidal lining epithelium, a single layer in thickness for the most part. Also, columnar-celled alveoli, some containing colloid, are present (×150).

On March 6, 1950, the operation was performed.* Through the usual thyroid exposure, a normal right lobe of the thyroid was demonstrated. A cyst about the size of a golf ball presented in the lower pole on the right, and was attached near the inferior parathyroid gland. It was translucent, had a delicate wall, and contained clear fluid. It was removed intact. The patient recovered uneventfully.

At pathologic examination the specimen consisted of the thin wall of a large cyst measuring approximately 5 cm. in diameter. At one portion there was a small piece of pink tissue. The question had arisen at operation as to the probability of this being a parathyroid cyst. The cyst wall showed only fibrous tissue without an epithelial lining. Continuous with this wall was definite parathyroid tissue composed of both chief and oxyphil cells (Fig. 2).

CASE 3 (J. H. H., 162875).—A 43-year-old obese Negro woman complained of a swelling in the neck present for seven years. The mass, which had been the "size of a marble"

*By Dr. Edward Stafford.

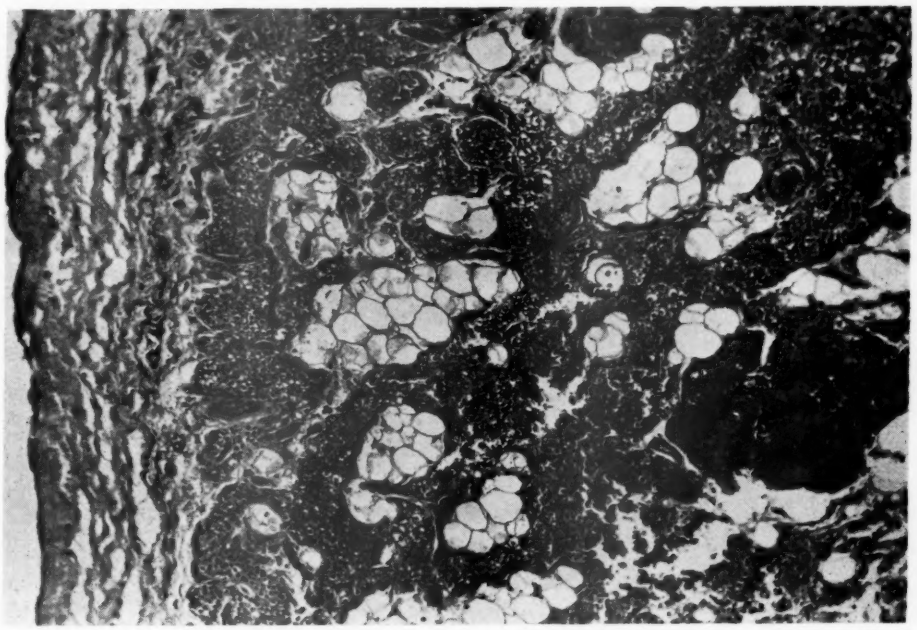

Fig. 2 (Case 2).—Parathyroid tissue in the wall of the cyst. The fibrous cyst wall, devoid of epithelial lining, is at the far left. Fat is present in the parenchyma, which is made up mostly of chief cells, with a cluster of oxyphil cells seen at the far right (×150).

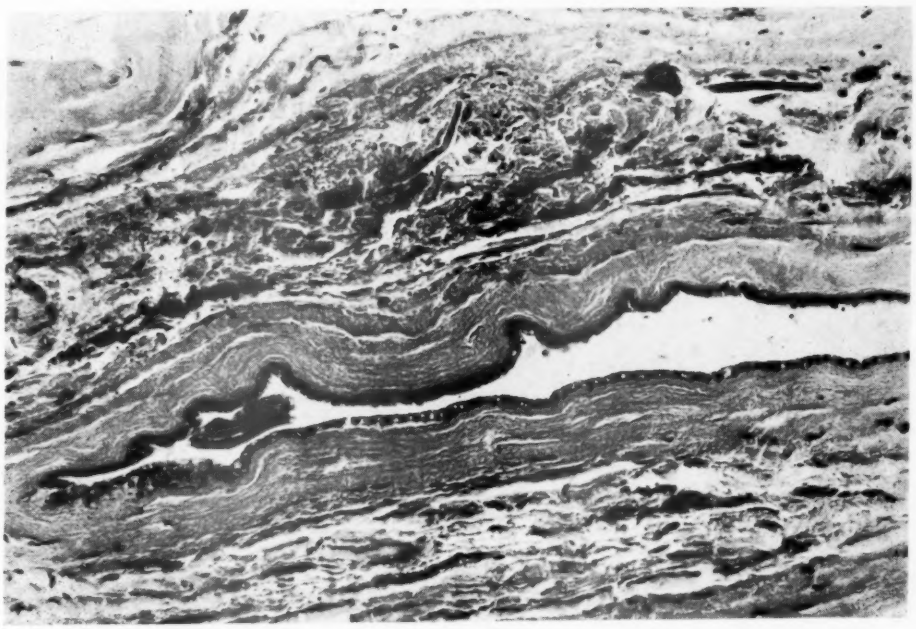

Fig. 3 (Case 3).—The cyst wall folded upon itself. Cuboidal lining cells, resembling chief cells, are on a dense connective tissue layer. In other portions of the cyst wall typical parathyroid parenchyma is embedded both within and just outside the dense connective tissue layer (×250).

when first noted, had grown steadily. Nevertheless, it was essentially asymptomatic. There was no suggestion of thyroid or parathyroid hyperactivity.

On examination, a 3 by 4 cm. firm lobular mass was found to occupy the region of the left lower pole of the thyroid. It was nontender and rose in the neck with swallowing, its lower border extending behind the sternum. The operation was performed* on Sept. 3, 1950, and the palpable mass proved to be a translucent, thin-walled cyst arising from the lower pole of the thyroid and measuring 3 by 3 by 4 cm. in size. The cyst was readily removed with its contents. Pathologic examination again showed a cyst with a uniform thin wall. Histologically, it was lined by a single layer of flattened cuboidal or rectangular cells with a surrounding zone of fibrous tissue (Fig. 3). In the wall of the cyst parathyroid tissue was embedded (not illustrated).

TABLE I

AUTHOR	SEX	AGE	LOCATION OF CYST	SIZE	INDICATION FOR OPERATION
Goris (1906)	M	22	Left lower pole of thyroid	(Three closely applied cysts)	Mass in neck, goiter?
Anzilotti (1909)	M	25	Right inferior parathyroid gland	"Egg-sized"	Branchial cleft cyst
de Quervain (1925)	F	55	Anterior superior mediastinum (left)		Substernal thyroid adenoma derived from left lobe of thyroid gland
Nylander (1929)	M	16	Between sternomastoid and angle of mandible on right	"Goose-egg sized"	Cervical cyst; branchial cleft origin?
Welti** (1946)	F	53	Region of left inferior parathyroid		Goiter
McKnight (1946)	M	17	Lateral aspect of the lower left thyroid lobe	"Golf-ball sized"	Goiter
Black and Watts (1949)	F	32	Behind and distal to inferior pole of left lobe of thyroid	4 cm. diameter	Goiter
	M	30	Position of right superior parathyroid	1 cm. diameter	Hyperparathyroidism (adenoma weighing 200 mg. removed from left superior parathyroid followed by clinical remission)
Cooley and McGoon (1951)	M	66	Right inferior parathyroid region	4 by 2 by 2 cm.	Hyperthyroidism with adenomatous left lobe of thyroid
	F	49	Right inferior parathyroid region	5 cm. diameter	Goiter (adenoma of right lobe of thyroid)
	F	43	Left inferior parathyroid region	3 by 4 cm.	Goiter (adenoma of left lobe)

**Welti stated that he reported another case of parathyroid cyst in 1932, but gave no reference, and we have been unable to locate such a report.

DISCUSSION

Including the patients in this report, there are only eleven similar cases recorded in the literature. For the usual reasons, many have undoubtedly not been reported. An analysis of the reported cases of parathyroid cysts is summarized in Table I. These cysts may occur in any decade of life. The youngest

*By Dr. Richard F. Kieffer.

and eldest patients were 16 and 66 years old, respectively. The sex incidence is approximately equal.

All but three of the parathyroid cysts have been located in the region of the inferior parathyroids, and of unique interest is the consistent description by the surgeon of the loose attachment of the cyst to the lower thyroid pole, with great ease encountered in separation of the cyst from the thyroid. The three atypical locations of the cysts are as follows: in the position of the right superior parathyroid, in the anterior part of the superior mediastinum (probably having been displaced with a substernal adenoma of the left lobe of the thyroid), and between the sternomastoid muscle and the angle of the mandible. The sizes of the cysts have varied from 1 to 5 cm. in diameter.

Of interest in regard to the predilection of the cysts for the inferior parathyroid glands are the investigations of Gilmour.[1] In 428 autopsies he discovered only 11 cysts which were visible to the naked eye and all were located in the lower glands. Earlier authors were also aware of this greater frequency in the lower glands.[1,2]

No specific symptomatology may be ascribed to parathyroid cysts. There is no known correlation between the occurrence of the cysts and the physiologic activities of the parathyroid tissue. In the one patient in whom clinical hyperparathyroidism was confirmed, a typical parathyroid adenoma weighing 200 mg. was removed from the opposite side. In no instance has tetany followed surgical excision. The appearance of the cyst in conjunction with hyperthyroidism in one of our cases is probably coincidental. Welti[7] called attention to the possibility of vocal cord palsy from interference with the recurrent laryngeal nerve. This finding may be considered exceptional. The ultimate fate of these cysts is unknown, but for the present they should be considered as simple space-occupying lesions.

In most of the cases, cuboidal or flattened cuboidal epithelium has lined the cyst space, with the parathyroid tissue embedded within the connective tissue capsule, though the epithelial lining has not been a constant feature. Other than the size, there is often little to differentiate the common microscopic type of cyst from the rarer large type which has surgical importance. Gilmour has studied the parathyroid gland extensively and his findings have been corroborated in our own autopsy material. In the adult gland there are usually scattered changes in the essentially patternless structure of the parenchyma. There may be columnar-celled alveoli (Fig. 1) resembling the alveoli of a secreting gland or similar alveoli filled with colloid, which, when accumulated in larger amounts, distends the alveoli and forms true colloid vesicles (Fig. 4). Still further development to larger sizes gives rise to cystic vesicles which are more irregular in shape and have a flatter lining epithelium (Fig. 5). In areas adjacent to normal parenchyma, the vesicles may lose their connective tissue support and thus lose the distinctness of the epithelial lining (Figs. 5 and 6). Some of these cysts found in routine autopsy material may reach quite large proportions (Fig. 6), and may have had hemorrhage into them.

The origin of these pathologic structures which we call parathyroid cysts is not clear. The proposed explanations resolve into two possibilities; namely, that the cysts are formed by retention of secretions in the frequently encountered colloid vesicles within the gland[9]; or that they are derived from those developmental remnants located near the gland or incorporated within it, which can ultimately be traced in origin to the third or fourth pharyngeal pouch.[6, 10, 11, 12] Since this second proposal is at least as plausible as the first, it is with hesitation that one labels as a parathyroid cyst a structure which is possibly derived from a pharyngeal pouch remnant, which becomes located near the parathyroid gland, and only secondarily incorporates the parathyroid within its wall. In fact, reports have been made of the surgical removal of cysts in the region of the parathyroid glands which resemble the reported parathyroid cysts, but which have no demonstrable parathyroid tissue in their walls. Black and Watts[2] mention four such cases, and Welti[7] reports three more.

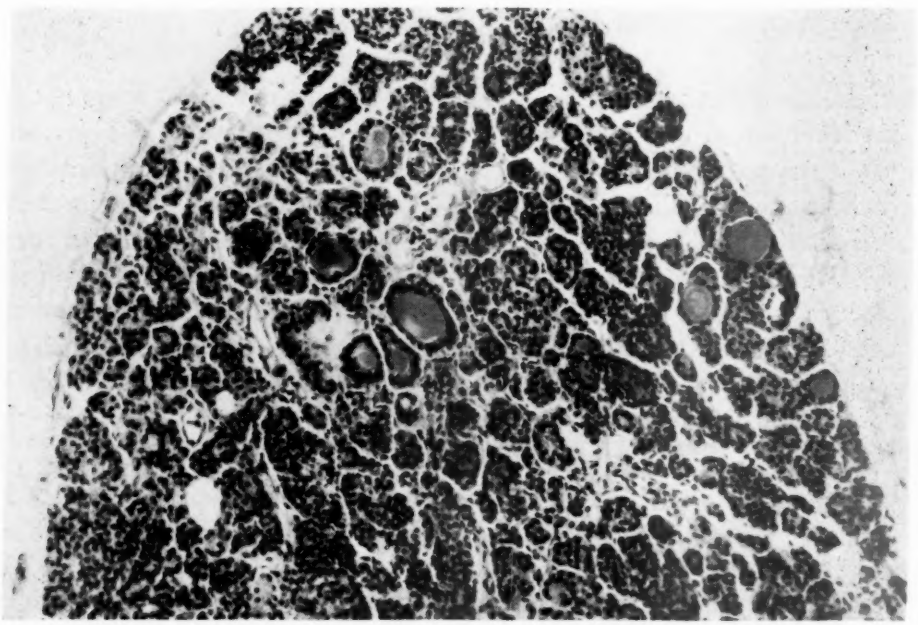

Fig. 4.—A portion of a parathyroid from a routine autopsy. Colloid vesicles, more distended than the alveoli in Fig. 1, are present in an otherwise typical gland (×200).

Though a more accurate name than "parathyroid cyst" might thus be desirable, this term has descriptive value and denotes a rather distinct entity, which commonly has a characteristic location and relation to surrounding structures. It is for these reasons that the term is retained here. At present it is not justifiable to consider these cysts of strictly parathyroid origin.

Though the surgeon will but rarely operate upon a patient with a parathyroid cyst, this situation may prove puzzling when first encountered. Study of the reported cases, however, indicates that an awareness of its usual presentation should make it recognizable as such at operation in many instances. Thus, a thin-walled, tense cyst containing watery or slightly opalescent fluid,

Fig. 5.

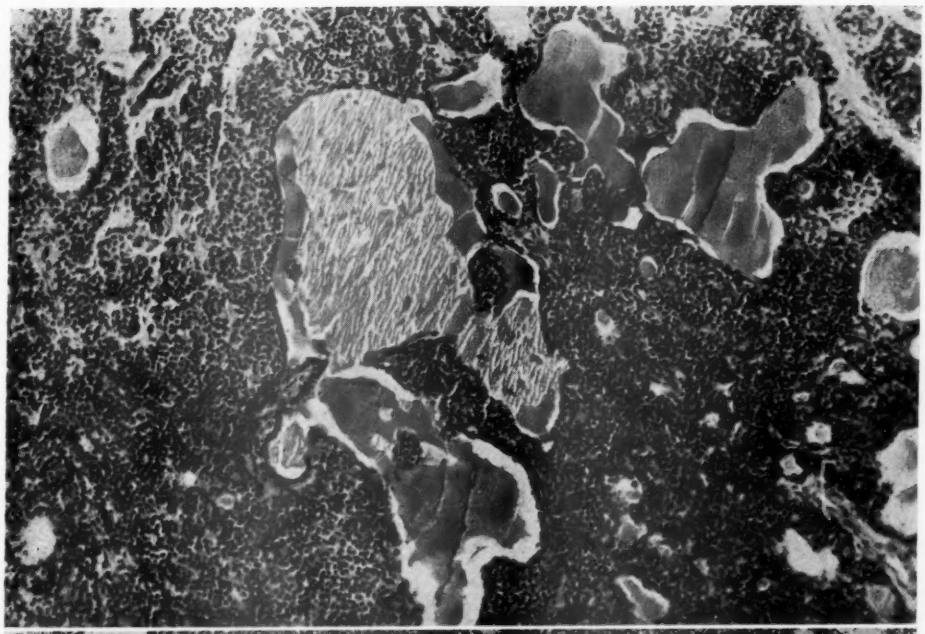

Fig. 6.

Fig. 5.—A parathyroid removed at autopsy. Large, irregular, cystic vesicles are surrounded by normal parenchyma which has not formed continuous, distinct, epithelial cyst linings (×150).

Fig. 6.—Still larger cystic vesicles in a parathyroid gland removed at routine autopsy (×50).

and attached to the posterior surface of the inferior pole of the thyroid, but easily separable from the thyroid, will in many instances prove to be a parathyroid cyst.

SUMMARY

Parathyroid cysts remain a surgical curiosity, yet their occurrence in microscopic size is commonplace. Their origin is not definitely established, they appear functionally of no significance, and are symptomatic only as space-occupying lesions. No known dangerous potentialities are attributable to them. Three cases of parathyroid cysts which were removed surgically are reported, and certain characteristics are discussed.

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SACROCOCCYGEAL TERATOMA IN INFANTS AND CHILDREN

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INTRODUCTION

THE sacrococcygeal tumors of early infancy have always aroused considerable interest and speculation, but relatively little is known of their natural history. The sacrococcygeal teratomas are among the commonest, if not the most common, large tumors seen in the first three months of life.[1, 2] We have followed 6 patients with pathologically proved teratomas of the sacrococcygeal region and have records of 3 further established cases. In two additional patients whose tumors were clinically characteristic of presacral teratoma pathologic studies are wanting. Two of our cases (Cases 6 and 7) have been previously reported by Lisco in 1942.[3]

Although we are aware of the close relationship of all teratomas, we have confined this report to those complex tumors located in the sacrococcygeal region, appearing at birth or shortly thereafter, and containing derivatives of 2 or more germ layers. We would differentiate such tumors[4, 5a] from (1) caudally attached incomplete (parasitic) twins which are distinguished by their external position and by evidences of development of a separate individual, from (2) supernumerary limbs and tails, and from (3) residues of postanal gut or duplications of the rectum—structures which can be shown histologically to contain only colonic epithelium and the normally occurring surrounding muscular coats and are in no sense teratomatous.

The literature on the sacrococcygeal teratomas is replete with descriptions of unrelated bizarre anomalies and the hand-me-down errors common to all medical literature. Thus the euphonious term "Middeldorpf" tumor has crept into usage to describe almost any tumor in the presacral region. A recent paper[6] stated "Middeldorpf in 1885 first reported a case of retroperitoneal tumor of the presacral area in a child wherein a teratomatous sacrococcygeal tumor arose from the postanal hind gut. Since that time many different types of tumors in this region have been called 'Middeldorpf' tumors. Adson, Moersch, and Kernohan[7] in describing chordoma of this region pointed out that dermoid cysts, fibrosarcomas, neurofibromas, ganglioneuromas, benign giant cell tumors of the bone, ependymomas and chordomas occurring in the pre-sacral region had each at one time or another been called a Middeldorpf tumor. Due

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to the diversity of types of tumors which arise in the presacral region it is suggested that such tumors be described primarily according to their structure and that if the term 'Middeldorpf tumor' is used it should be used only pre-operatively as a diagnostic aid, for a Middeldorpf tumor is strictly speaking a sacrococcygeal teratoma of the postanal hindgut.'' However, Middeldorpf[8] in fact reported a single case which appears to be no more than a duplication of the rectum. He described a 1-year-old female infant with a tumor near the anus and a natural opening in the tumor from which fecoid material discharged. The ''tumor,'' removed by Kraske, consisted of several loops of bowel communicating externally with the fistulous orifice. In one area of the tumor the mucosa was so fixed to that of the rectum that it could not be separated and this portion had to be left behind. The tumor was lined by mucosa with Lieberkühn crypts, with submucosa, circular and longitudinal muscle, but no serosa, and appeared similar to a segment of normal bowel embedded in fat and connective tissue. Middeldorpf went on to explain the origin of the ''tumor'' from the postanal hindgut, largely on a comparative anatomic basis. His own name and his embryologic explanation are all that persist of his original report. There seems little doubt that his patient had a duplication of the rectum and anus and Middeldorpf neither described a presacral teratoma nor any type of sacral neoplasm.

PATHOGENESIS

As the teratomas combine the problems of congenital abnormality with those of neoplastic growth, it is small wonder that the literature as to origin and cause of teratomas is confused by the widest speculation. Similar tumors occur very infrequently in lower species, the most common instance being the benign testicular teratomas of young horses.[5b] Experimentally teratomas have been produced in the testes of fowl by the injection of zinc sulphate.[9] In amphibian embryos the introduction of coagulated embryonic extracts, which are thought to contain those factors (evocators) responsible for tissue differentiation but to lack those responsible for the coordination of the growth as a whole, will induce the formation of chaotic tissue developments somewhat resembling those seen in teratomas.[9]

In our present state of ignorance only general assumptions as to the natural origin of these tumors can be made. Several theories still in acceptance should be discarded,[5a] however, on the basis of recent embryologic advances and the excellent pathologic studies of Nicholson.[10a] Among these unsubstantiated hypotheses are those suggesting the development of teratomas from fertilized polar bodies, from misplaced blastomeres, and from wandering sex cells. The idea that the migration of primitive sex cells may cause mediastinal or sacral teratomas is given no support by the recent work of Witschi,[11] who traced the normal path of migration of the primitive human sex cells from the yolk sac. The hypothesis that sacral teratomas may represent cases of fetus in fetu was disclaimed by Budde[12] and subsequently by other workers.[5, 10] A fetus in fetu can only enter the body of a host through the vitelline duct; it should present

evidences of membranes or a blood supply befitting its indentity, and it should show some evidences of metameric segmentation. These criteria are all lacking in sacrococcygeal teratomas.

Teratomas might be considered to result if embryonic tissue, potentially able to produce many varieties of tissue, were to escape from the influence of forces normally responsible for the coordination of its growth and development into structures characteristic of the mature organism. At present it cannot be said whether the fault lies primarily in the factors providing stimulus for coordination of the differentiation of the tissue or with abnormal changes in the response of the tissue focus to a normal stimulus. Developing tissue exhibits several characteristics of its growth—an advance in the direction of cellular maturity, maintenance of the pace of increase in size, and coordination with its neighboring tissues and organs. The teratomas develop into mature and sometimes into functional adult cells, and also enlarge with the body, but they are out of step with the normal cadence. In small areas as instanced by a tubule of respiratory epithelium surrounded by cartilage and muscle, they may show evidence of local tendencies towards organization of adult tissue, but the over-all picture is one of uncoordinated confusion. In some cases a different change in pace and character of growth occurs in certain of the cells in a teratoma, producing a malignant growth. It is of interest, however, since teratomas are so generally considered to be abberations from the normal, beginning in presomite and early somite stages, that except for the account of Gruenwald[13] no tissues suggestive of teratoma formation are reported in embryos or fetuses previous to the sixth month.

CLINICAL HISTORY

We have reviewed 39 published cases reported since 1938 to which we have added our 9 cases in an effort to determine something of the clinical history of the tumors under discussion. The cases previous to 1938 have been reviewed by Chaffin[1] and others.[14, 15, 16] As in Chaffin's series, we find a decided predominance in females. There were 32 females out of 46 children in whom the sex was given. All of our own proved cases occurred in white children despite the large number of Negro admissions in the Johns Hopkins Hospital. One of our patients without pathologic studies was a Negro. Of the total of 48 proved cases, 45 were listed as white, one as Puerto Rican,[17] and one as Japanese.[18]

While in most reports the scanty family history and casual account of the pregnancy give evidence of the lack of importance attributed to these features, the recent discoveries of Gregg,[19] Warkany and associates,[20] and Gillman and colleagues[21] make this aspect of the history in any congenital abnormality a matter of increasing importance.

The cases showed no significant age distribution of the parents, although less than one-half the histories gave information on this point. A history of twinning in the family was recorded in 3 cases. One of our patients was a twin, and though both of these twins were females, no note is made as to whether or not they were identical twins. In only 4 cases of 48 was note made of the mother having had previous abortions or stillborn children. In one of

these cases the stillborn sibling had been anencephalic. The pregnancy was described as normal in 15 cases and definitely abnormal in 4.[22-25] Three of the 4 had toxemias. Two of our cases were premature, conceivably in association with the increased expansion of the uterus to accommodate the huge tumor. There are cases of marked dystocia due to the size of the tumor, one case resulting in the death of the mother despite the dismemberment of the fetus.[24]

One striking finding in the clinical histories of the children and infants with these tumors is the common occurrence of an avoidable delay in establishing a correct diagnosis. Five cases were misdiagnozed for lack of a rectal examination which would have revealed the existence of the tumor. When the performance of a rectal examination is so routine a procedure in the examination of patients of older age groups, it is difficult to understand the failure to include it in the routine examination of infants.

The chief symptoms which were present were as follows: Complaint of a mass occurred in 38 patients. The tumor varied externally from one which was 44 cm. in diameter to a 2 cm. "birthmark" in the skin.

Obstruction of the rectum and constipation were noted in 10 cases. Four of these patients had gross bleeding with defecation.

Urinary obstruction requiring catheterization occurred in 9 cases with rupture of the bladder and peritonitis in one of these.[26] Two additional cases originally presented other symptoms but had urinary obstruction after malignant recurrence. That urinary obstruction can be present very early is underscored by our Patient 9, in whom it was found at premature birth in the seventh month.

Pain or discomfort was present in 7 cases. The child sometimes showed a preference in lying or sitting in one or another position which may have antedated the external appearance of an obvious tumor mass.

Infection occurred in 6 cases with sinus formation in 4. The infection may develop spontaneously with external rupture of the tumor through necrotic skin into the rectum (Case 1). Infection has also occurred subsequent to incomplete excision of the tumor (Case 8).

Endocrine activity has been reported by Rhoden[27] in 1 case as a cause of precocious puberty. All of the tissues in a teratoma are potentially functional, but whereas endocrine symptoms are relatively common in terotomas of the testis, they appear to be rare in presacral teratomas. The occurrence of gonadal tissue in these teratomas has not been established.

The duration of the symptoms varied from less than 1 day to 21 years. The appearance of malignancy did not seem to be correlated with the duration of symptoms or with the size of the tumor. The majority of the tumors, 31 cases recorded, were present at birth, and 1 of our patients died with a large tumor on the day of a premature (seventh month) delivery (Case 9).

PHYSICAL EXAMINATION

The tumor mass was visible in 43 cases, and not apparent externally in 5. Other congenital abnormalities were noted in 8 cases and included a 3 lobed

left lung,[24] a meningocele with spina bifida,[28] 2 imperforate anuses,[25, 26] 1 genital abnormality,[29] 1 case of club-foot,[30] and 1 simple spina bifida.[31] One patient (Case 4) was mentally defective. Calcium within the tumor was demonstrated by roentgenogram in 16 cases. It is to be noted that destruction of the sacrum may occur as the result of pressure erosion by a benign tumor, as in our case (Case 8). Hormone studies in the 1 endocrinologically active case revealed presence of androgen production.[27] This tumor had identifiable areas of adrenal cortical tissue.

DIFFERENTIAL DIAGNOSIS

Clinically the following tumors should be differentiated:

Meningoceles.[32]—Posterior meningoceles are always associated with a spina bifida. Pressure changes may be transmitted to the fontanels if they are open. The posterior meningocele is usually covered with a mere membrane. A meningocele is uniformly cystic unilocular, and shows no tendency to spread through the buttocks. Patients with meningoceles usually show neurological disturbances which are rare in teratomas. Anterior meningoceles are rare and show the same qualities of consistency and transmission of pressure on rectal palpation of the tumor as posterior meningoceles. It must be remembered that a presacral teratoma may exist in a child who has a meningocele.[28]

Neurogenic Tumors of Pelvis and Perineum.—These tumors, if situated behind the rectum, may be clinically indistinguishable from the teratomas. They are less likely to elevate the coccyx and sacrum posteriorly and are more likely to bulge into the perineum. On palpation the tumors are nodular and firm, and lack x-ray evidence of calcification.

Chordomas.—These tumors tend to occur in older patients and are found within the pelvis or higher, rarely showing extension into the buttocks. They may show evidences of destruction of the sacrum.

Hemangiomas and Other Tumors of the Buttocks.—Occasionally a large cystic hemangioma of the buttock may appear to arise within the pelvis, but rectal examination will show it to be confined to the buttock. These tumors may involve the skin as well.

Aspiration biopsy is unwarranted and probably poses some danger of dissemination of the tumor. Myelography also seems unnecessary but if a meningocele can be eliminated in no other way, dye may be introduced in the subarachnoid space above and an attempt made to recover it below.

COMPLICATIONS

Pressure.—Obstruction of the rectum, obstruction of the urethra and compression of the ureters against the pelvic brim, necrosis of the skin, and fistula or sinus formation all may result directly from pressure of the large tumor mass.

Infection.—Infection in the tumor may result from necrosis of the tumor and ulceration of the skin or rectum, or may occur as a result of incomplete operative removal with immediate or delayed wound breakdown. The chronicity

of the infection and its severity may be so debilitating as to lead to the death of the child (Case 8) without development of any actual malignancy.

Malignancy.—Chaffin[1] gave the incidence of malignancy as 9 per cent in his 72 cases reviewed. In the 48 cases of the present group there are 8 instances of malignancy, an incidence of 17 per cent. The danger of malignancy has generally been minimized, whereas it should, in fact, constitute one of the chief reasons for removal of these tumors in early infancy.[3] The malignant change may be seen even at birth, but in the present group appeared to be most often recognizable about the tenth month of life. The external size of the malignant tumors varied from a "birthmark" to a large external tumor. The size and character of the external portion of the tumor, therefore, gave no index as to its ultimate nature. The malignant tumors usually present complications by the time that they are first seen, as in 7 of the 8 cases reviewed. Five showed obstruction to the rectum and 4 showed urinary obstruction. Of these 8, 6 were explored, and in 4 the tumor appeared to be completely extirpated. All 4 of these tumors were considered benign on pathologic examination, but metastases subsequently occurred in each case. The recurrences are usually first seen locally in the sacrum, in the pelvis, or in the buttocks. Recurrences usually occurred about 7 months after resection, the earliest in less than 1 month. Death in the 8 cases occurred in 1 to 11 months. The longest reported latent period before a recurrence after resection is 2 years.[33] Metastases pass to the inguinal and iliac nodes and to the pre-aortic and mediastinal nodes. The liver and lungs are frequently invaded. Brain metastases have not been reported. Visceral metastases have appeared before there was evidence of local recurrence.

The cellular type of malignancy is most often a papillary adenocarcinoma. Four cases were so described, and 2 others called "adenocarcinoma." Other microscopic diagnoses were embryonal carcinoma and undifferentiated carcinoma.

TREATMENT

When the tumor has presented an obstetrical difficulty so that puncture for decompression has been necessary, removal of the tumor should be carried out as soon as possible since the neonatal fecal discharge carries a low or negligible bacterial content and operation may be undertaken before infection occurs.[34] A newborn infant tolerates the operative procedure as well as an older child.

Operation is indicated as soon as the diagnosis has been made, due regard being given to the general status of the patient and any local infection. Preoperative irradiation is unwise because of the usual resistance of teratomas[35] to irradiation and because of the problems introduced by irradiation of the pelvis, sterilization of the gonads, and interference with the epiphyses. If the child is a poor risk and the tumor large, a few days of transfusion and chemotherapy will produce as much improvement as can be hoped for without removal of the tumor. The feasibility and relative safety of performing extensive resections in infants, with constant transfusion during operation and adequate postoperative care, is shown by our cases and those of Sulamaa and Ahvenainen,[2] who operated upon 7 patients with such tumors without an operative fatality.

OPERATIVE PROCEDURE

As with all major surgery in infants a leg vein is cannulated for continuous transfusion. The tumor is approached from the posterior aspect with the patient supine and the pelvis elevated on folded towels. The anus is draped out but left accessible. A vertical elliptical incision is made so as to excise most of the redundant skin with the tumor. We have found it a great convenience to have an assistant place a finger in the rectum to elevate the tumor into the wound and to minimize the danger of injury to the rectum. A rubber balloon in the rectum will serve the same purpose almost as well.

The dissection is carried peripherally with excision of the tumor en bloc, leaving the sacral attachment to the last. Bleeding is best controlled with the cautery, and care must be taken in the region of the attachment to the sacrum, where the main blood supply to the tumor is usually derived from the lateral sacral arteries, which are secured before division. It is simplest usually to resect the coccyx as was done in 11 of the cases reviewed, and if necessary a portion of the sacrum may be taken as well. The presacral area should be palpated for other segments of the tumor which may not show a gross connection with a more caudal or dorsal portion of the tumor. The importance of this is illustrated by the case reported by Renner and Goodsitt[36] in which a benign postsacral teratoma was removed, only to have subsequent malignant development in a teratoma anterior to the sacrum.

In cases in which a fistula exists between the rectum and the tumor, as in our Case 1, it has been suggested that preliminary colostomy may be performed.[37] However, in the present instance, excision of the tumor and closure of the fistula was achieved without colostomy and without infection. Primary closure is possible in almost all cases except when infection has required excision of a large area of skin.

Suggestion has also been made of a combined abdominal and sacral approach if the tumor should prove too large or too extensive for a simple posterior excision.[37] We have not found this necessary in a sacrococcygeal teratoma, but have employed it in resecting a large anterior meningocele associated with a presacral dermoid. In that instance the tumor was dissected free from above and delivered by the sacral route. Because of the large dead space within the pelvis after removal of a presacral teratoma, the presacral space should usually be drained and a pressure dressing applied.* It may be of value to have the patient lie on the abdomen after operation, particularly to prevent fecal soiling of the wound. Repeated aspiration may be required if the dead space fills with fluid.

In cases in which malignant change has been found in the excised tumor, postoperative irradiation may be of value, but it appears to be largely symptomatic and palliative. At present the only hope of cure appears to be early and adequate resection.

*In a newborn infant operated upon after this paper was written, the cystic presacral teratoma was found to be dumbbell-shaped. The constriction was caused by the bony pelvic ring and the intra-abdominal portion was larger than the pelvic portion. Successful delivery was effected through the usual posterior incision.

RESULTS

In 1938, Chaffin[1] published the following results obtained in 45 cases in which resection of the tumor had been performed:

TABLE I

RESULT	PER CENT	NO. OF CASES
Recovery	57.7	26
Died	24.4	11
No report	17.9	8
Total cases		45

In the period 1938 to 1950, including the present report, the following results have been found in the 39 reported cases and the 9 reported here:

TABLE II. RESULTS OF TREATMENT

No treatment (or exploration alone)		
Stillborn		5
Exploration alone		1
Died without treatment		3
Irradiation alone		
Irradiation with death from tumor		2
Surgical resection (six with irradiation)	(total,	37)
Survived and well		25
Operative deaths		2
Died with intercurrent disease		2
Died because of benign tumor recurrence		3
Died because of malignant tumor recurrence		5

The operative results shows some improvement over those reported earlier. The deaths of 3 patients from tumors which were histologically benign serves to point out the great dangers from infection or obstruction which these large tumors may cause even though benign. It is also to be noted that incomplete excision of 2 apparently benign tumors was followed by growth of a rapidly fatal malignant recurrence.

PATHOLOGY

These tumors are generally large and often of really great size, as that in our case 9: a 640 gram tumor in a child of 1,900 grams. A few of the tumors are small presacral cysts not visible externally. Most of the tumors are cystic, frequently being composed of one large cyst with subsidiary smaller cysts. Though not found in our cases, "organoid" elements such as metatarsal bones, segments of intestine complete with serosa and mesentery-like blood supply have been reported.[10b] Masses of tissue which are recognizable grossly as brain tissue have also been reported. Teeth, skin, and hair are well-known findings. The tumors usually have a well-differentiated dense fibrous capsule with a tough fibrous adhesion to the sacrum. On gross section the cysts may be found to contain serous or mucoid material and cartilage and bone may be identifiable.

Microscopically there is a hodge-podge of tissues of all sorts jumbled, intermingled, and growing in and completely around each other in the greatest confusion with rarely a focus simulating local orientation. The tissue elements of

a teratoma are often distinguished by bizarre characteristics reminiscent and suggestive of adult tissues yet unlike any specific tissue they might seem to resemble. Epithelial elements in particular show a large variety of glandular and ductlike structures variously lined by ciliated, by mucus-producing, or by stratified epithelium or by combinations of these. The glial tissue rarely can be identified any more closely than as being from the central nervous system, although ganglion cells, ependyma, and choroid plexus may be seen. Embryonic and adult tissues exist side by side although, with the exception of mesenchyme-like connective tissue, fat, and types of nervous tissue, the histology is more often that of adult types of tissue, usually atypical and only suggestive of one type or another of adult tissue or structures. The more commonly found tissues are squamous epithelium and skin appendages, brain and glial tissue, intestinal mucosa, cartilage, fat, and striated muscle. The histologic findings are given below in the 48 cases reviewed.

Epidermis	39
Oral mucosa	6
Dental tissue	1
Lens, eye choroid	1
Brain and glial tissue	25
Ganglia	6
Peripheral nerves	13
Choroid plexus	10
Intestinal mucosa	34
Liver	1
Pancreas	5
Respiratory mucosa	18
Urinary tract	5
Genital tract	1
Mesenchymal tissue	13
Connective tissue	26
Cartilage	27
Bone	14
Fat	25
Striated muscle	22
Smooth muscle	13
Cardiac muscle	1
Lymph tissue	9
Adrenal	2

CASE REPORTS

CASE 1.—V. K. (JHH No. 444575), a 4-day-old girl, was admitted for a tumor of the buttocks (Fig. 1). She was the first child of 30-year-old parents. It was noted that delivery was complicated by retarded rotation and forceps were applied.

Physical Examination.—The child seemed well except for a great tumor mass deforming both buttocks, elevating the coccyx dorsally, and displacing and stretching the anus anteriorly. The skin over the tumor was healthy, but the tumor was soft and fluctuant in many areas, with firm areas palpable within it. Rectal examination showed the pelvis largely filled by the great tumor.

Operation.—On Dec. 6, 1947, a generous vertical ellipse of skin was taken with the tumor, which was removed with the coccyx. Separation from the rectum was aided by the finger of an assistant in the rectum. The tumor was encapsulated and did not appear to invade the tissues. Healing was per primam, and the child was discharged 9 days later at the age of 15 days.

Pathologic Report.—The tumor measured 95 by 80 by 50 mm., weighed 214 grams, and consisted of a group of adjacent, attached nodular masses, the largest of which was 50 mm. in diameter. Some of the nodules on section were composed of small cystlike structures

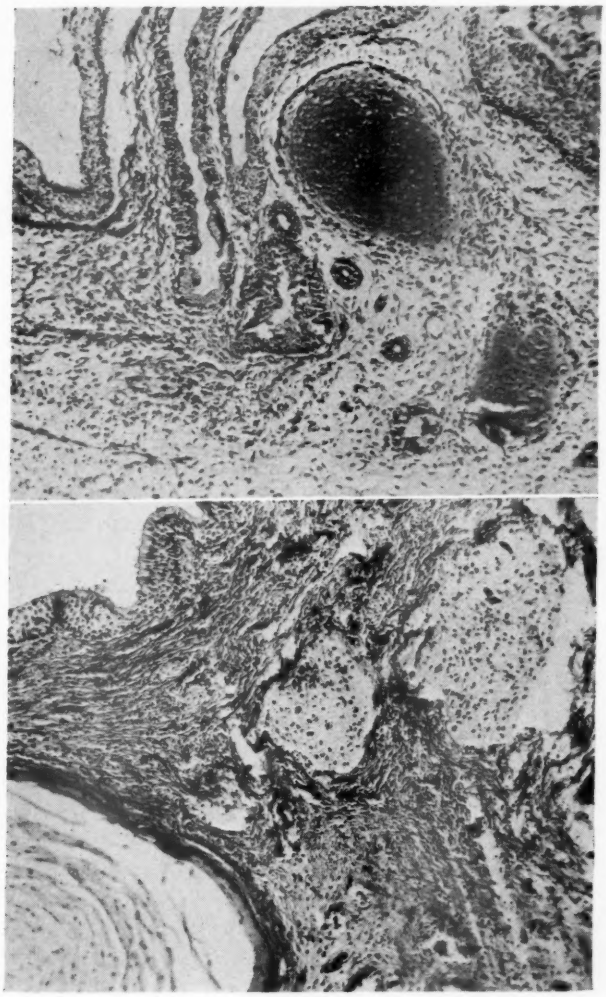
A. *B.* *C.*

Fig. 1 (Case 1).—V. K., a 4-day-old baby girl with large sacrococcygeal teratoma. There was operative removal, per primam healing. *A* and *B*, The tumor is a huge deforming rubbery cystic mass elevating the coccyx, displacing and stretching the anus. *C*, The displacement of coccyx and sacrum is plain in the roentgenogram. There are a few small areas of calcification.

filled with a material like mucus. Some of the smaller nodules were denser and contained large proportions of connective tissue. In one of them some bone was grossly recognizable. One small cyst gave the appearance grossly of being lined with intestinal mucosa.

The sections showed a great variety in the microscopic picture. One area showed a peculiar loose, almost myxomatous, stroma in which there was cartilage and a calcified material within the cartilage which was not definitely bone. Near by was a cystlike structure containing what appeared to be desquamated keratin, and lined by tall epithelium suggestive of the respiratory tract. In another area glands lined by goblet cells and by ciliated columnar cells were seen, while others had squamous epithelium. All of these elements merged into one another. Fairly respectable hair follicles were seen, and also a few areas of striated muscle.

D.



E.

Fig. 1.—*D*, Photomicrograph (×100). In a loose stroma suggesting mesenchyme there is an island of cartilage and a number of ductlike structures variously lined by stratified squamous epithelium, by ciliated columnar epithelium, and by goblet cells. Two or three fairly regular structures suggest hair follicles. *E*, Photomicrograph (×100). In the lower left corner is a cyst lined by a flattened squamous epithelium and filled with what appears to be desquamated keratin. In the upper left is the edge of a cyst lined by ciliated columnar epithelium. The two lighter areas to the right suggest glial tissue. (Photomicrographs reduced one-third.)

Summary.—A female infant had a large presacral teratoma resected when she was 6 days old. She left the hospital 9 days later, healed and well. She is well 2½ years later.

CASE 2.—Baby K. (HLH A59439) was brought to the hospital at the age of 5 days with the sacral tumor noted at birth (Fig. 2). No abnormality of pregnancy or delivery was reported.

In the sacrococcygeal region was a huge mass tilting the sacrum and coccyx dorsally and displacing the anus caudally and ventrally. The mass, about 10 by 15 cm., appeared to be entirely cystic. The skin over the most distal portion of the tumor was discolored and almost necrotic.

Operation.—On Dec. 6, 1947, a large area of skin over the mass was excised with the tumor. The tumor was densely attached to the coccyx, which was removed with it. A distended Foley bag catheter in the rectum aided delivery of the tumor and dissection of the rectum. The tumor was well encapsulated.

Pathologic Examination.—The specimen was a large cyst, thin walled and containing a thin yellow fluid. The cyst wall was 2 mm. in diameter and attached to its inner surface were a number of small cysts filled with mucoid material. Microscopic sections showed stratified squamous epithelium with some hyperkeratosis. Beneath it were occasional sweat glands, hair follicles, and nerve trunks. Here and there were striated muscle bundles and islands of fairly mature cartilage. In one area, papillary projections were covered by small cells with dark-staining nuclei which suggested ependymal cells. One small area contained glial tissue. The stroma varied from loose connective tissue to frankly myxomatous tissue. There were many large blood-filled spaces.

The child left the hospital on the seventeenth postoperative day with the wound healed per primam.

Summary.—In a 5-day-old baby girl a thin-walled cystic presacral teratoma was so large as to produce necrosis of the overlying skin. Removal was accomplished without incident and healing was per primam. The child is well 2½ years later.

CASE 3.—C. J. (HLH A 54274) was brought to the hospital at the age of 5 months because of a sacral tumor present since birth. He was the second child of healthy young parents. His mother had had a dermoid cyst of the ovary removed one year previously. Although pregnancy and delivery were normal, and the child's weight was 6 pounds, 10 ounces, he soon showed evidence of marked cerebral defect. The mass which had been noted over the buttock on the second day of life increased in the next 5 months as the child grew. No obstruction to urination or defecation had been noted.

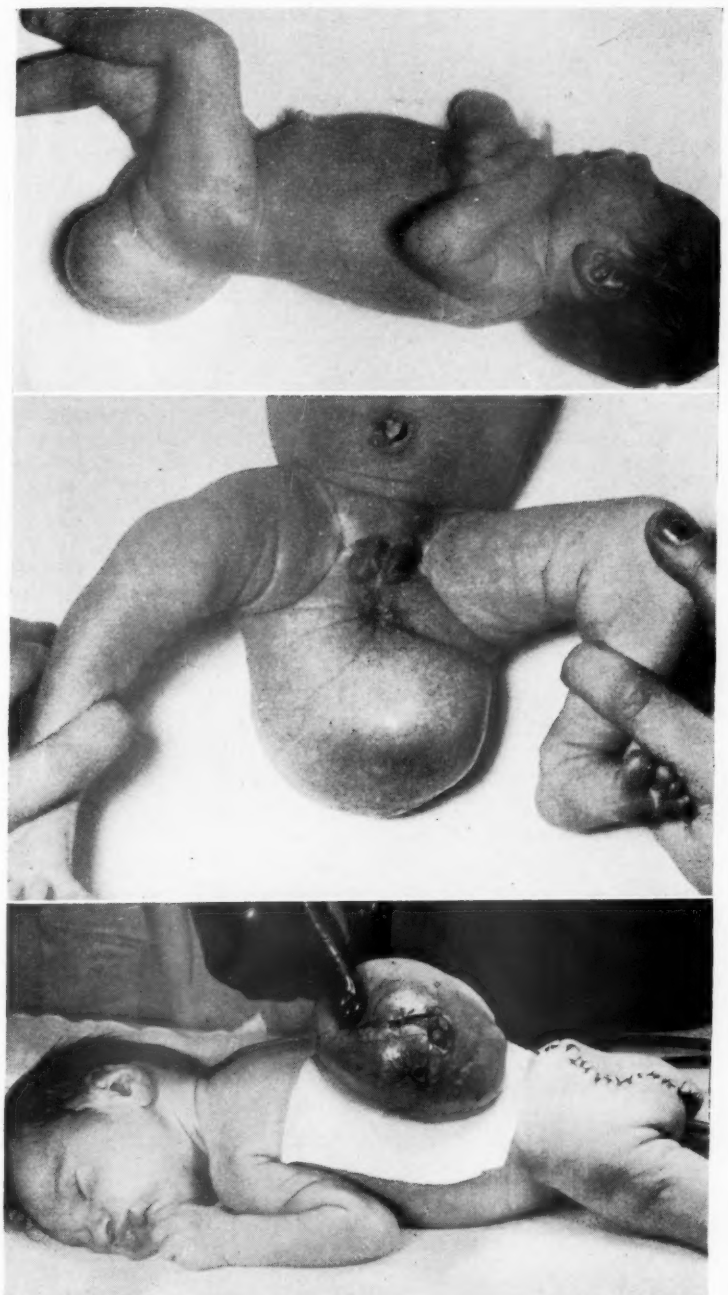
Physical Examination.—On admission the child showed evidence of mental retardation. There was a visible bulge just below the sacrum elevating the coccyx dorsally. On rectal examination the mass could be felt bulging into the rectum as a smooth, round, cystic tumor.

Operation.—On March 27, 1947, the tumor was delivered through a posterior midline incision. An assistant's finger in the rectum aided in the delivery of the tumor and in its separation from the rectum. The coccyx was removed with the tumor, which was well encapsulated and densely adherent to it. The wound healed per primam.

Pathologic Examination.—The tumor consisted of a completely encapsulated mass 7 cm. in its greatest diameter. There were several cystic areas varying from 5 cm. to 1 cm. in diameter. Several pieces of bone were recognizable grossly. There were several small processes of very firm consistency.

Microscopically many types of tissue were identifiable. In several areas there was dense connective tissue, while in others squamous epithelium was seen to line cyst cavities. Other smaller cysts were lined by ciliated columnar epithelium characteristic of respiratory

epithelium. Also present was mucus-producing columnar epithelium, which resembled that seen in the lower intestinal tract. Bone was present, as were islands of rather mature cartilage. No histologic evidence of malignancy was seen.



A.

B.

C.

Fig. 2 (Case 2).—Baby girl K, a 5-day-old baby with a large, thin-walled, cystic presacral teratoma. The posterior surface of the tumor was already cyanotic and necrotic. Resection of the tumor was followed by per primam healing. *A* and *B*, The tumor is characteristic of the large teratomas which are visible externally almost in their entirety. *C*, The tumor has been removed with a large disc of attached skin. The central gangrenous area of skin is visible. The incision was closed and a pressure dressing applied. In a number of instances fluid collects and aspiration is required. The catheter in the rectum was used to inflate a balloon elevating and demarcating the rectum during the dissection.

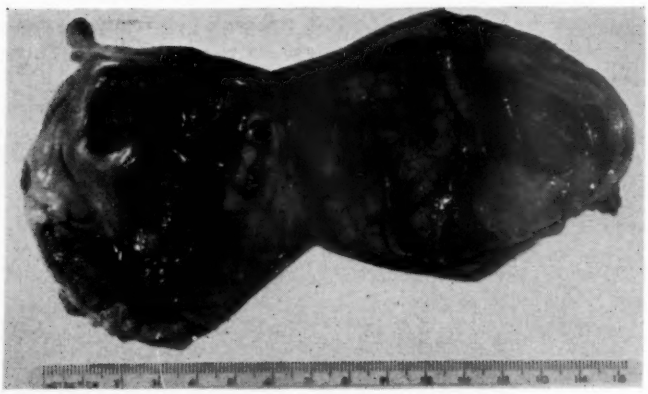
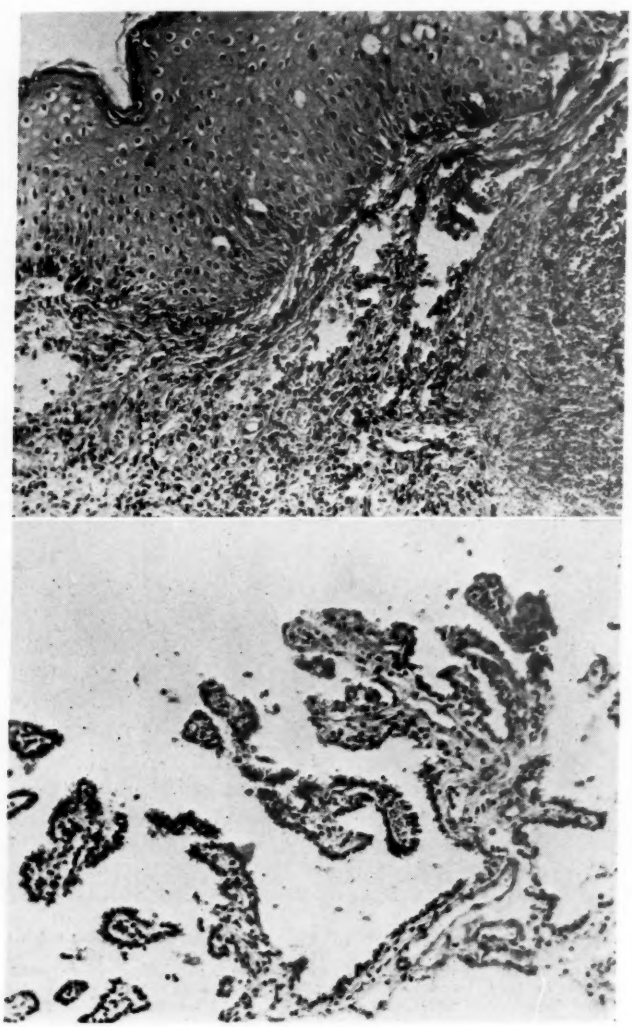


Fig. 2, *D*.—Most of the teratomas are solid with large and small cystic areas. In this instance, however, there is essentially one large thin-walled cyst with a few thickened areas in the wall.

E.



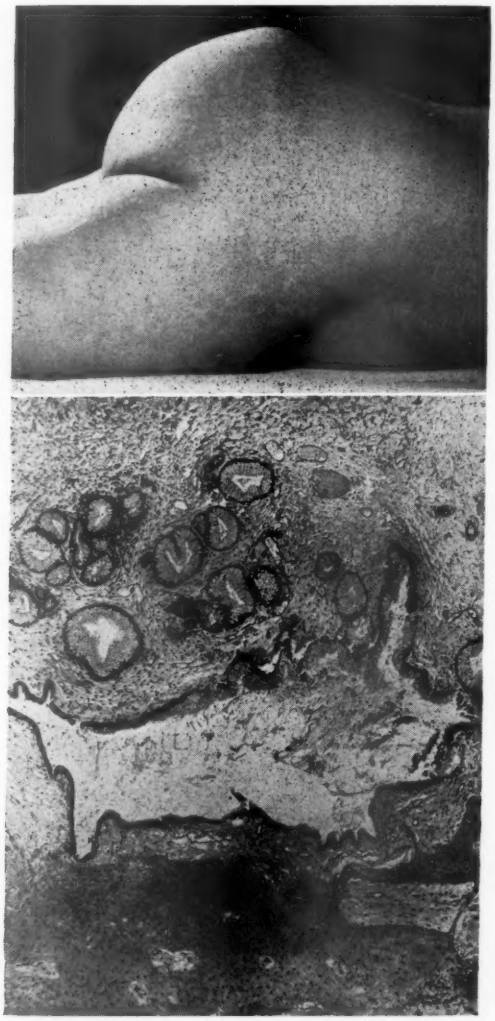
F.

Fig. 2.—*E*, Photomicrograph (×150) of cyst wall showing keratotic squamous epithelial lining. *F*, Photomicrograph (×150). In this section the loose villiform structure is strongly suggestive of the choroid plexus. (Photomicrographs reduced one-third.)

Course.—The patient was readmitted with pneumonia a few weeks after discharge and responded to sulfadiazine and penicillin. In September, 1947, he was admitted to another hospital with high fever, still an obvious mental defective with spasticity of the extremities. He succumbed on Oct. 8, 1947, and autopsy showed no evidence of recurrence of the presacral tumor, the previous site of which was represented by a well-healed scar.

Summary.—A 5-month-old boy had been noted to have a sacral swelling at birth. Operative removal of a typical presacral tumor was accomplished uneventfully. The child was severely defective mentally and succumbed at the age of 11 months. Autopsy showed no recurrence of the tumor.

A.



B.

Fig. 3 (Case 3).—C. J., a 5-month-old baby boy with sacral swelling noted since birth. There was no evidence of growth of the tumor and no history of pressure symptoms. Resection was done, and was followed by primary healing, but serous fluid had to be aspirated on several occasions. *A*, Lateral view, indicating dorsal tilt of sacrum. *B*, Photomicrograph (×100). Curious appearing glands lie in a loose stroma, some areas of which strongly suggest glial tissue. (Photomicrograph reduced one-third.)

CASE 4.—F. P. (JHH No. 494911), an 8-year-old girl, was admitted because of a draining swelling on the buttocks present since infancy (Fig. 4). She was the second child of healthy parents. The pregnancy had been normal although delivery was by a breech presentation. At birth the patient was noticed to have a cherry-red area in the sacral region. When she was 5 months of age this area began to drain and was operated upon elsewhere with the diagnoses of spina bifida and meningocele. After the operation the area drained purulent material constantly. Occasional walled-off collections of pus required additional incision and drainage. Development was normal and there had been no neurological signs or symptoms.

Physical Examination.—The child was a vigorous 8-year-old girl. Over the lower part of the sacrum was an extensive healed scar with several persistent sinuses marked by foci of dirty granulation tissue. On rectal examination one could feel a doughy mass posterior to the rectum and pressure from within the rectum expressed creamy pus through the sacral cutaneous sinuses. X-ray showed an incomplete fusion of the first sacral segment with a small defect. There was a soft tissue mass posterior to the sacrum. Radiopaque material injected into the sacral sinuses demonstrated an apparent connection between the sinuses and the rectum (Fig. 4). It was felt that the child had a presacral teratoma, infected by previous operation, with a fistulous communication with the rectum secondary to the infection. It was conceivable that the infection derived originally and spontaneously from the rectum.

Operation.—On March 23, 1949, the entire scarred and infected area of skin and fat was excised down to the gluteal muscles and the rectum. The coccyx was removed together with the large, firm, discrete presacral tumor which was densely attached to the sacrum 1 cm. above the junction with the coccyx. This portion of the sacrum was rongeured away. The sinus was followed down and proved to enter the rectum. The fistulous tract was excised and the rectum closer over. Decision was made not to perform a proximal colostomy.

The wide excision of infected tissue precluded closure of the cutaneous defect. The wound was packed with dry gauze and the patient treated with penicillin and streptomycin. Twenty days later clean granulations had sufficiently filled the deep hollow to permit successful application of small deep grafts. The defect was completely healed by May 15, 1949. One year later the wound remains nicely healed.

Pathologic Report.—The subcutaneous mass consisted of rather curious-looking fat and fibrous tissue in which were numerous cystic spaces containing cheeselike material and hair.

The microscopic examination showed a great diversity of tissues. Glial tissue was conspicuous in many areas; in others were typical apocrine sweat glands, and in still others fairly normal cartilage. Bundles of striated muscle and curious, abnormal nerve fibers appeared in some areas. Quite close to an area showing cartilage and nerve tissue were hair follicles, sweat glands, sebaceous glands, and apocrine glands in a peculiar stroma of fat and dense connective tissue. The glial tissue was patchy in little areas here and there and the various skin derivatives seemed abnormal. There was a sinus tract lined by ciliated columnar epithelium.

Summary.—An 8-year-old girl had a reddened area on the sacrum at birth. An operation undertaken for cure of a "meningocele" resulted in persistent infection and drainage. Wide operative resection of sinuses, infected skin, and presacral tumor and closure of a rectal fistula were followed by grafting of the resultant defect. The patient is well a year later.

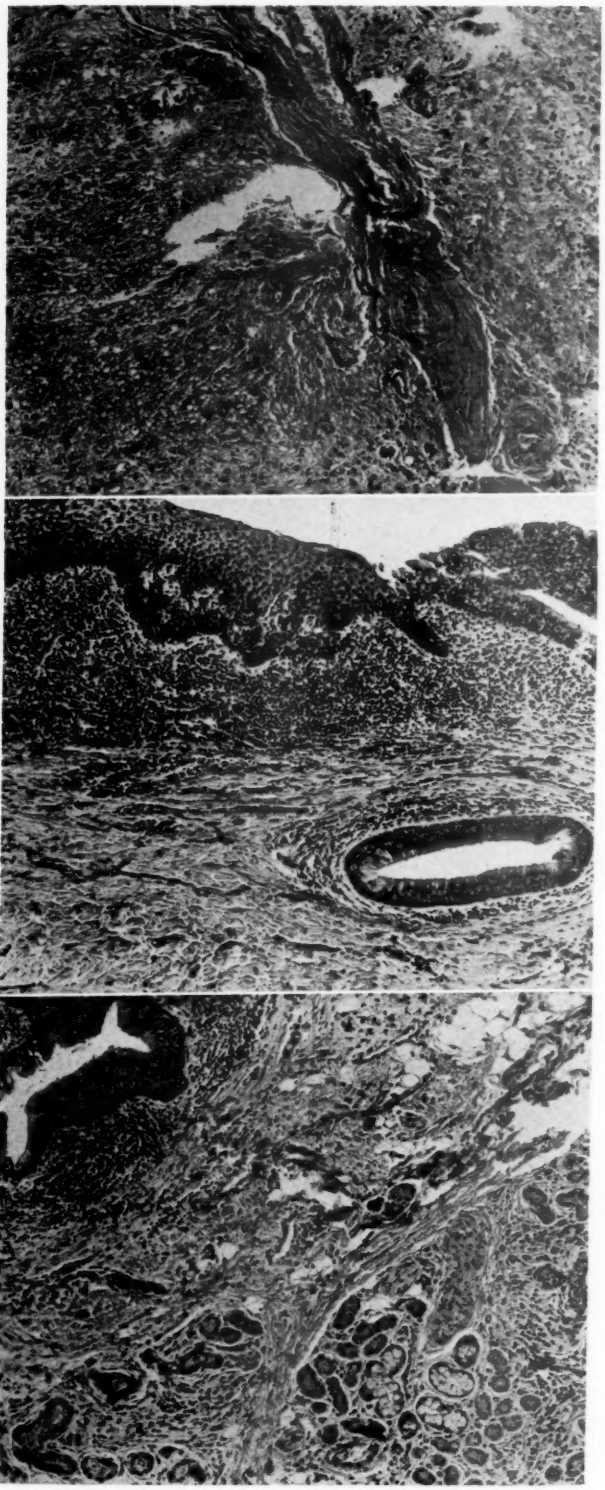
CASE 5.—R. C. (HLH A-55105) was referred, at the age of 1½ years, for a recurrent tumor of the buttock. The second child of normal parents, he weighed 7 pounds 11 ounces at birth after a normal delivery. Nothing abnormal was noted about the pelvis until 6 weeks before admission, when a lump was noted in the left buttock. A physician found a 5 cm. mass, fixed in the depths of the left gluteus, impinging upon, but not fixed to, the anus. In one week the mass increased 50 per cent in size. Aspiration biopsy then undertaken showed a highly cellular neoplasm and irradiation was begun. He received 1,750 r in 7 treatments and the mass seemed to disappear. However, a week later the child began to strain at stool, developed difficulty in defecation, and was now found to have a mass high up posteriorly on rectal examination.

A.

B.

C.

Fig. 4 (Case 4).—F. P., an 8-year-old girl with a small discolored area on the buttocks which was present at birth and drained constantly after an operation for what was thought to be a meningocele. *A*, There are multiple dirty draining sinuses in a shiny, diffusely inflamed, sacral swelling. *B*, Lipiodol injected into one of the sacral sinuses passes freely into the rectum. *C*, Result one year after wide resection of the presacral teratoma and infected soft tissues. The opening into the rectum was closed, the wide soft tissue defect packed open, and the granulating wound subsequently covered with small deep grafts.



D.

E.

F.

Fig. 4.—*D*, Photomicrograph (×100). One of many areas of typical glial tissue. This one contains a band of dense fibrous tissue. *E*, Photomicrograph (×100). A sinus lined by squamous epithelium showing intense chronic inflammation and immediately beneath it a duct lined by tall columnar epithelium. *F*, Photomicrograph (×100). Various types of glandular structures are dispersed in a loose stroma in which there are also areas of fat and what appear to be nerve fibers. (Photomicrographs reduced one-third.)

Physical Examination.—Examination showed a vigorous, well-appearing child. There was a grayish brown discoloration of the left buttock and on rectal examination a smooth, soft mass 5 cm. above the anal sphincter, round and extending upward about 4 cm., was evident. It was rather firmly fixed to the surrounding tissues but was not hard.

Operation.—On May 19, 1947, a soft mushy tumor 2 cm. in diameter was found almost directly beneath the skin over the coccyx. The tumor was resected with coccyx, subcutaneous fat, and a good deal of the left gluteus maximus muscle which contained a dense mass of yellow scar tissue, apparently the irradiated tumor. A large cystic portion of the tumor passed anterior and superior to the sacrum. It was removed in toto—postcoccygeal tumor, coccyx, gluteal tumor, presacral tumor. It was then possible to feel several rubbery nodes high in the pelvis, obviously metastatic tumor quite separate from the original mass and quite beyond the reach or hope of surgical attack.

Pathologic Report.—All sections showed tumor. In some areas bizarre glandular structures and cysts were lined by respiratory, squamous, or completely atypical epithelium. There was one body that looked like a corpuscle of Vater-Pacini, other glands that suggested breast or prostate, with here and there strands of peripheral nerve tissue. In some areas there was frank cancer with all the characteristics of adenocarcinoma: irregularly formed acini and irregularly sized cells, large and variable with hyperchromatic nuclei.

Course.—Healing was per primam and the child was discharged for further x-ray therapy. He next was admitted to the Children's Hospital in Boston, Sept. 25, 1947, with a palpable mass about the sacrum and pulmonary metastases demonstrated radiologically. Nitrogen mustard therapy caused a disappearance of the shadows in the chest roentgenogram but the rectum remained solidly encased by tumor in the pelvis and the liver continued to enlarge. He died (Jan. 22, 1948) at home, and autopsy was not performed.

Summary.—A sacrococcygeal teratoma without an external mass in a 1½-year-old boy was first manifested by malignant invasion of the left buttock and gluteus maximus. Irradiation shrank this extension, but rectal examination still revealed a typical cystic mass. An extensive operation with resection of the primary tumor disclosed high intrapelvic metastases. Pulmonary, hepatic, and intra-abdominal metastases developed. Nitrogen mustard therapy temporarily improved the appearance of the roentgenograms of the chest. Death occurred when the child was 2 years old. There was no autopsy.

Case 6.—E. Y. (HLH A98937), the fifth child of young parents, was noted the day after birth to have one buttock larger than the other. The swelling grew rapidly and by the time the baby was 2 months old the anus was distorted, stretched, and pouting, and the mucosa tended to prolapse. Shortly before the patient's admission to the hospital, at the age of 10 months, the stools had become ribbon like.

Physical Examination.—When admitted on Sept. 21, 1936, there was a great, smooth, but firm enlargement of the right buttock extending caudally and medially. The skin over it was warm, and large veins were visible over it. The sacrum was tilted dorsally. Rectal examination through the stretched and distorted anus showed a smooth, rounded mass displacing the rectum far to the left. Roentgenogram showed calcification of the tumor.

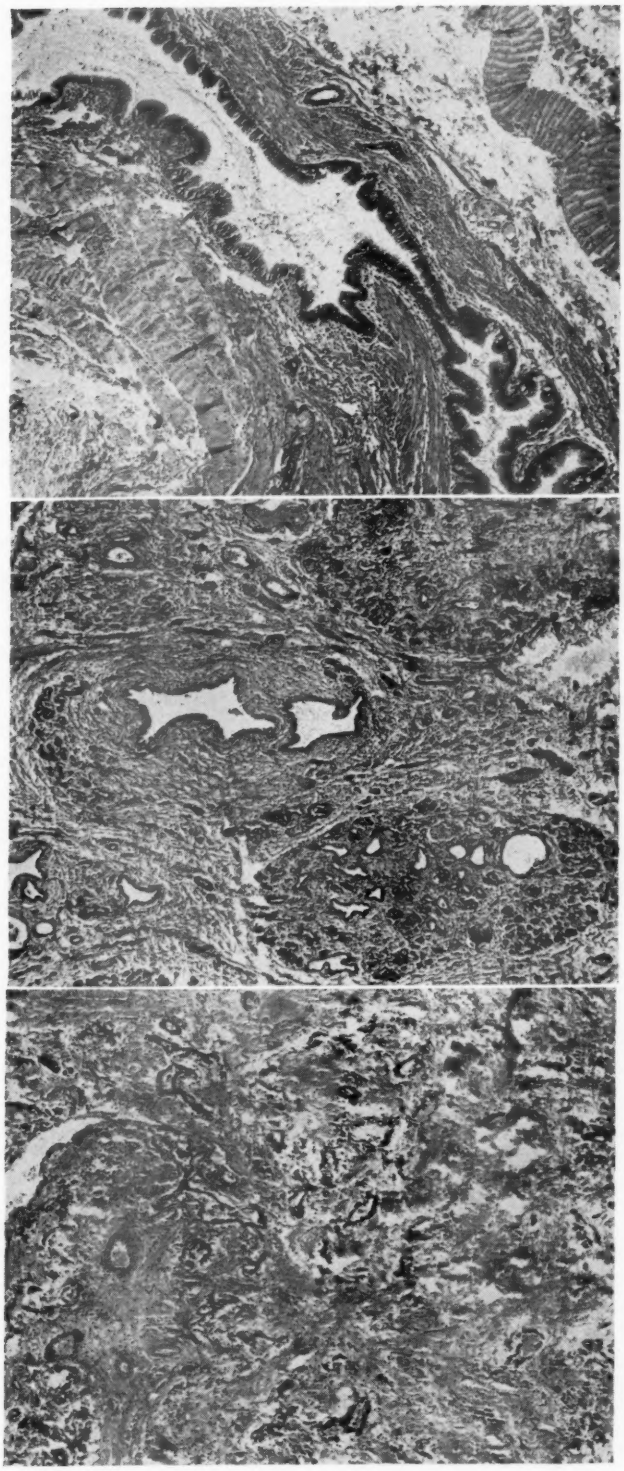
Preoperative irradiation was elected and a total of 1,740 r administered. The child was permitted to leave the hospital and was readmitted in February, 1937, when the tumor was larger still, the anus was displaced far to the left, and paralysis and flaccidity of the legs had developed.

Operation.—On June 18, 1937, despite the great size of the neglected tumor and the poor condition of the child, the operation was well tolerated. The tumor was found to consist of one principal mass and a number of discrete subsidiary masses. It was thought that all masses were removed, but tumor attachments to the sacrum had to be curetted.

Pathologic Examination.—The tumor removed measured 12 by 10.5 by 10 cm. It was surrounded for the most part by a fibrous capsule. On section there were many varied cysts. A few calcified foci, areas of dark pigmentation, sebaceous material and hairs were identifiable.

Microscopically the cysts were lined by various types of epithelium—ciliated and nonciliated cylindrical epithelium such as resembles trachea, cuboidal or flat epithelium. Mucous glands were noticeable in the stroma, also cartilage and bone, smooth muscle, pancreas with islands of Langerhans, choroid plexus, and nervous tissue. In the base of the tumor was seen the

Fig. 5 (Case 5).—R. C., a 1½-year-old boy. A mass in the left buttock had been noticed only 6 weeks before and disappeared after irradiation, only to be followed by difficulty in defecation and demonstration of a presacral mass. *A*, Photograph of operative specimen. The large tumor was still discrete, but after it was removed inaccessible tumor masses could be felt high in the pelvis, and there evidently were metastases. *E*, Pulmonary metastases demonstrated 4 months after operation when the child was 22 months old. Pelvic and abdominal masses developed and the child died of cachexia at the age of 26 months. No autopsy was performed.



B.

C.

D.

Fig. 5.—*B*, Photomicrograph (×60) of a benign area of the tumor. A long ductlike structure is lined by a tall columnar epithelium with occasional goblet cells. The curiously ruffled ribbon of tissue suggests smooth muscle. *C*, Photomicrograph (×60). Whorls of fibrous tissue surround groups of glands and acini suggesting breast tissue. Scattered about the entire field are small sections of peripheral nerve tissue. *D*, Photomicrograph (×60). The apparently malignant area of the tumor suggests an adenocarcinoma with ill-formed glands, individual cells from which stream out into the tissue. (Photomicrograph reduced one-third.)

single type of cell which was malignant, large, polygonal, with pale-staining nuclei with little chromatin and scant cytoplasm. The tumor had the appearance of a papillary adenocarcinoma.

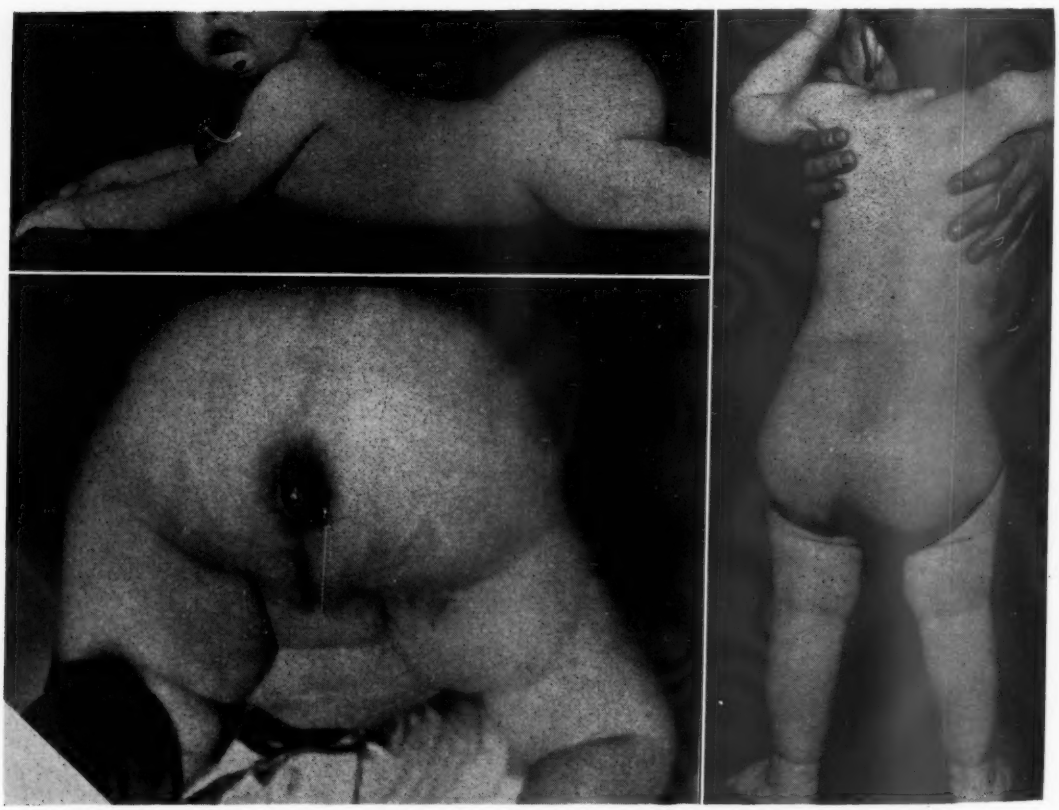
The wound never healed completely, and within a month an intra-abdominal tumor mass was palpable. This grew rapidly, cachexia increased, and the child died Aug. 21, 1937, at the age of 20 months.

Autopsy.—The body was that of an extremely emaciated and dehydrated female baby. A large pelvic and retroperitoneal tumor mass, continuous with a smaller tumor in the buttocks, displaced the pelvic organs, the aorta, ureters, and inferior vena cava anteriorly and superiorly. The main tumor was cystic and soft. It had eroded the vertebrae, intervertebral discs, and right ilium. Metastatic nodules were present in the lungs, liver, and bronchial, portal, and retroperitoneal lymph nodes. There was urethral and ureteral obstruction, with acute and chronic pyelitis on the right.

Microscopically the tumor was composed of the malignant elements which have been described previously in the operation specimen.

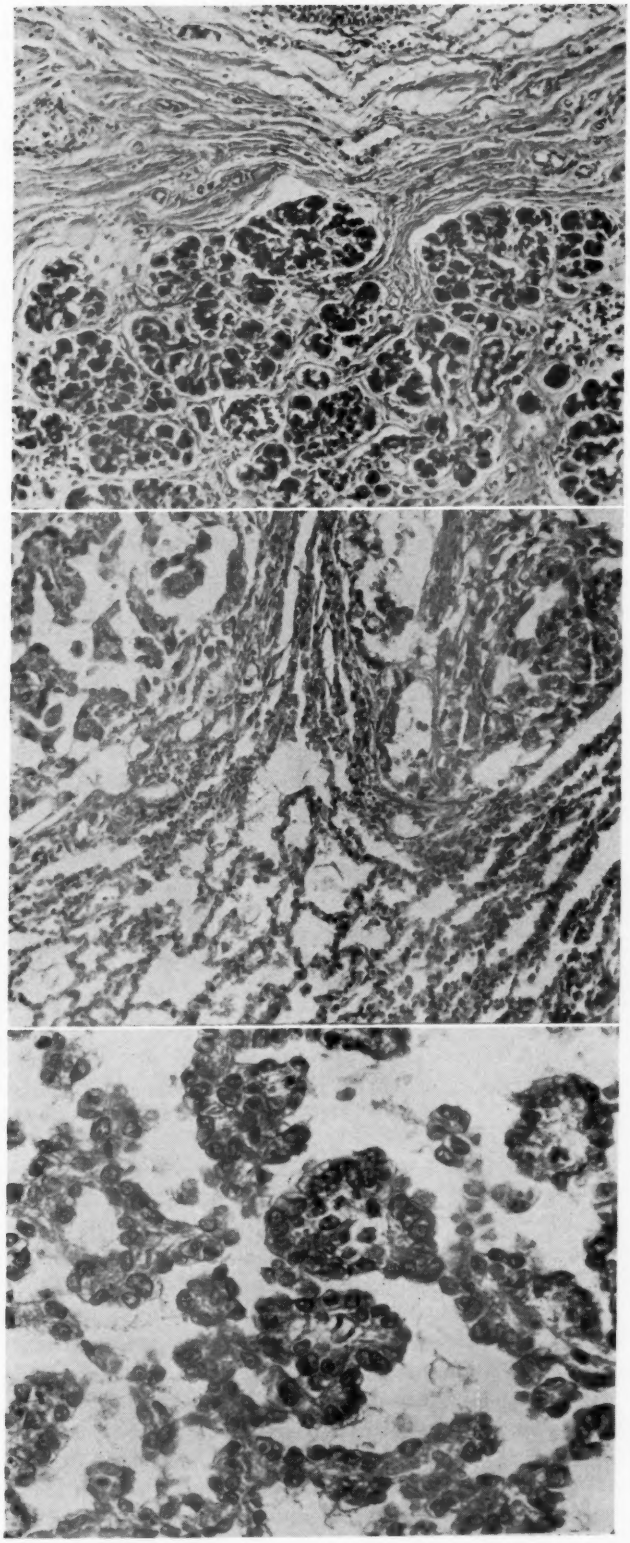
Summary.—Irradiation therapy was attempted in a 10-month-old child with a rapidly growing presacral teratoma. A few months later, despite paralysis

A.



C. *B.*

Fig. 6 (Case 6).—E. Y., a 10-month-old girl, had a tumor present at birth which was known to have grown rapidly since. Resection was performed at 19 months. The child died at 20 months of local recurrence and metastasis. *A* and *B*, The tremendous size of the tumor is apparent. Despite the great size of the tumor and its rapid growth the child's general condition was still good. However there was already marked compression of the rectum and the stools were ribbon like. *C*, The anus is stretched and distorted. Through its patulous orifice one can see the tumor bulging ventrally against the rectum. A lateral roentgenogram demonstrated the dorsal elevation of the sacrum and coccyx, and the presence of numerous areas of calcification in the tumor.



D.

E.

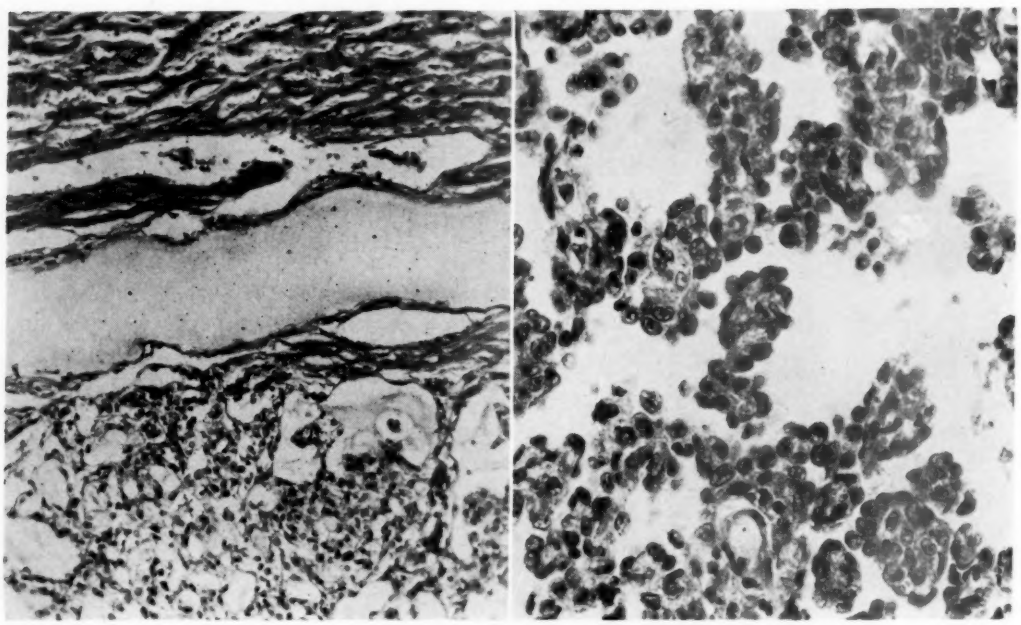
F.

Fig. 6.—*D*, Photomicrograph (×150). Taken from recurrent pelvic portion of tumor at autopsy. There is nothing suggestive of malignancy in this area. The well-formed mature glandular tissue shows in cytology and architecture the arrangement and character of either salivary glands or pancreatic tissue. There were no islands of Langerhans. *E*, Photomicrograph (×150) of pulmonary metastasis. Two areas of metastatic papillary tumor are poorly demarcated. One of the metastases seems actively spreading. *F*, Photomicrograph (×400). Enlargement of an area from the pulmonary metastasis in Fig. 6, *F*. Despite the fairly regular arrangement of this papillary tumor, the wide variety in nuclear cell types and the readily visible mitoses are indicative of the rapidly growing character of the tumor. Photomicrographs reduced one-third.)

of the extremities and cachexia, operation was attempted and the gross tumor was removed. Abdominal metastases were demonstrable within a month and the child died of widespread metastases at the age of 21 months.

CASE 7.—E. R. (HLH A50041) was admitted to the Harriet Lane Home at the age of 15 months on April 2, 1926, with complaints of constipation and retention of urine.

At birth he was noted to have a reddish discoloration to the left of the coccyx which was discounted by physicians. When the child was 3 months of age a lump appeared beneath the spot. At the age of 9 months the child began to have constipation. This increased progressively in severity and the left leg began to swell. Finally progressive urinary obstruction developed, requiring repeated catheterization. The child was then admitted to the hospital.



A. *B.*

Fig. 7 (Case 7).—E. R., a 16-month-old male child with a paracoccygeal discoloration at birth, a mass in the same area at 3 months, constipation at 9 months, swelling of the left leg, and progressive urinary obstruction. The entire pelvis was filled with a solid tumor. Death occurred from widespread metastases. *A*, Photomicrograph (×150), Autopsy section of hepatic metastasis. The tumor shows a loose arrangement of cells, forming open spaces suggestive of acini and containing what appears to be some sort of secretion. *B*, Photomicrograph (×400) of area from Fig. 7, *A*. Note the resemblance to the metastasis in Case 6 (Fig. 6, *F*). (Photomicrographs reduced one-third.)

Physical Examination.—A hemangioma-like purplish discoloration still existed to the left of the coccyx and a "walnut-sized" mass beneath it. Rectal examination done now for the first time showed a huge hard mass filling the left half of the pelvis and obstructing the rectum, from which now only ribbon stools passed. The lesion was thought to be a sarcoma and radiation therapy was advised. The intrapelvic mass decreased in size briefly but recurred. The inguinal glands enlarged and the liver became palpable. X-ray examination showed pulmonary metastases. The external mass had not increased in size when the child died on July 26, 1926.

Autopsy.—The body was that of an emaciated 16-month-old boy. A large tumor mass occupied the entire pelvis. Arising from the retroperitoneal space it displaced the normal organs anteriorly and superiorly. There was distinct continuity of the pelvic tumor with a smaller cystic area in the buttocks. The tumor had a continuous extension into the left thigh

but no invasion of bony structures. Metastases were present in the retroperitoneal nodes, liver, lung, and bronchial lymph nodes. There was also tumor tissue in the branches of the portal vein. Slight dilatation of the kidney pelvis was present.

Microscopic section of the cyst in the buttocks showed a lining of several types of epithelium: high columnar mucus-producing cells, ciliated and nonciliated cells, cuboidal cells. Hair follicles, nervous tissue, and smooth muscle were seen in the surrounding stroma. The malignant portion of the tumor showed it to be composed of somewhat cuboidal cells, with little cytoplasm and large irregular nuclei with many mitoses. They showed a papillary arrangement, although solid columns and small acini were also noticeable. Diagnosis was papillary adenocarcinoma.

Summary.—A male infant, in whom a reddish spot had been present at birth, a mass at 3 months, and constipation at 9 months, was treated with irradiation at the age of 15 months without success. Autopsy showed a malignant papillary adenocarcinoma developing in the presacral portion of a congenital teratoma.

CASE 8.—F. W. (A10047), a 4-month-old baby girl, was the abnormal member of a pair of possibly identical twins. She was admitted because of a sacral tumor which had been present since birth.

Physical Examination.—A thick tumor mass 10 by 4 by 4 cm. was present over the sacrum and hanging down behind the buttocks. It was soft and fluctuant, but contained material of bony hard consistency. Roentgenogram showed calcification within the tumor.

Operation.—At operation on May 16, 1927, difficulty was experienced in separating the tumor from the sacrum and from the rectum. In both regions it was thought that tumor tissue had been transected when the mass was delivered and removed.

Course.—An obvious recurrence of the tumor was noticed in the perineum while the patient was still in the hospital and she was discharged July 16, 1927, to be given x-ray therapy as an outpatient. She was readmitted Sept. 23, 1927, feeble and cachectic with an extensive dirty ulcer from sacrum to vulva. She died the day after admission.

Autopsy.—Post-mortem examination suggested that death occurred in consequence of the ulcerated, infected tumor recurrence. The tumor was infected, as were the surrounding tissues. There was thrush of the pharynx, larynx, and esophagus, a diphtheritic colitis, and a generalized fibrinous peritonitis.

The tumor mass was 5 cm. in diameter, extending from just below the sacrum to within 1 cm. of the anus, which was displaced forward. The tumor bulged 4 cm. above the expected surface of the skin. The pelvic floor was pushed upward by the tumor which bulged into the pelvis behind the rectum. The pelvic viscera were pushed forward by the tumor. The peritoneum was intact.

The tumor was sharply circumscribed and though not definitely encapsulated was surrounded by a definite fibrous tissue layer and sharply marked off from its surroundings. On section the tissue was soft, almost gelatinous, and in areas translucent. In some areas firm tissue resembled cartilage. There was obvious infection near the surface.

Microscopic examination of the original tumor showed many ectodermal structures—teeth with enamel organs, skin, central nervous system tissue, medullated nerve fibers; and mesodermal elements—bone, striated muscle, and connective tissue. The stump of tumor left behind again showed ectodermal elements, a great deal of nervous tissue, tubular structures like bronchi, and in one area of nervous tissue, abundant neuroglia and what appeared to be choroid plexus. There were scattered epithelium-lined ducts and small cysts, often with ciliated epithelium, sometimes with goblet cells. Epithelial-lined spaces in the nervous tissue suggested ependyma. There was nothing anywhere in the tumor to suggest malignant change.

Summary.—Operation was deferred until this child was 4 months old and then an incomplete removal of the presacral teratoma was performed. Recur-

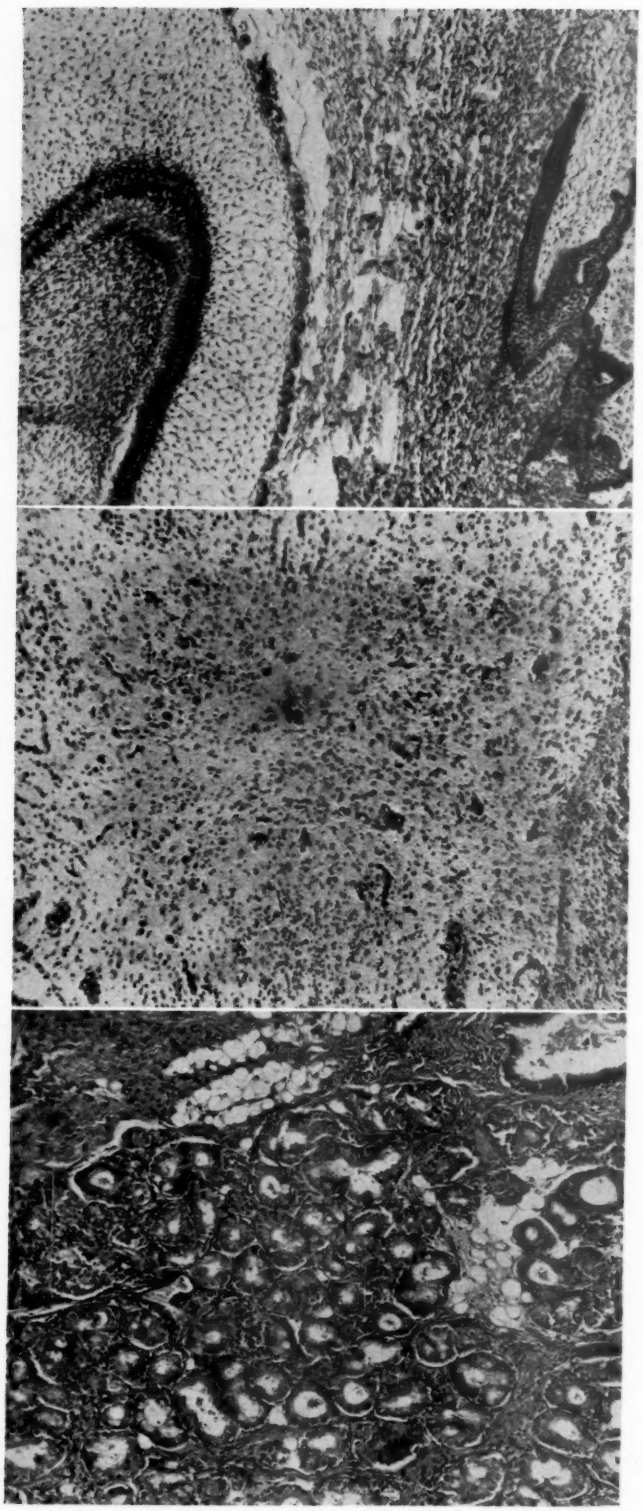


Fig. 8 (Case 8).—F. W., a 4-month-old infant, one of female twins. A large presacral tumor was present from birth. Incomplete removal of tumor was done, with immediate recurrence and death 4 months later at the age of 8 months. Autopsy showed a huge, ulcerated, infected pelvic tumor, apparently circumscribed and with no metastases. *A*, Photomicrograph (×100). This tumor contained many ectodermal derivatives. The enamel organ on the left is beautifully clear. On the right is an irregular arrangement of squamous epithelium and the tissue between seems to be smooth muscle. *B*, Photomicrograph (×100). One of many areas of what is obviously central nervous system tissue, in this instance, with ganglion cells. *C*, Photomicrograph (×100). Well-formed glandular tissue, fat, a larger cystic space lined by columnar ciliated epithelium. In other areas are cartilage, muscle, etc. (Photomicrograph reduced one-third.)

rence was almost immediate. Irradiation of the recurrence failed to affect the tumor, and ulceration and infection led to the death of the child. The tumor was still localized and still benign by criteria of gross and microscopic diagnosis.

CASE 9.—Baby S. (Autopsy 8144), died 1 hour after birth, and was brought to the hospital for autopsy. She was thought to be about a 7-month premature infant, weighing 1,900 grams and measuring 33 cm.

Autopsy.—There was a large tumor projecting posteriorly and caudally from the sacral region which was smooth, oval, and measured 13 by 9 by 9 cm. The tumor was nodular and extended into the perineum, stretching the skin between the anus and vagina. The tumor was firm in some areas, cystic in others. There were nodules of tumor in the left thigh.

The tumor weighed 640 grams and was attached to the sacrum. It was multilocular and had thick-walled septa, and variously contained solid, cheesy, and cystic portions. Some cystic tumor nodules were found along the muscles attached to the left femur. Pressure on the ureter in the pelvis had produced hydroureter and extreme hydronephrosis.

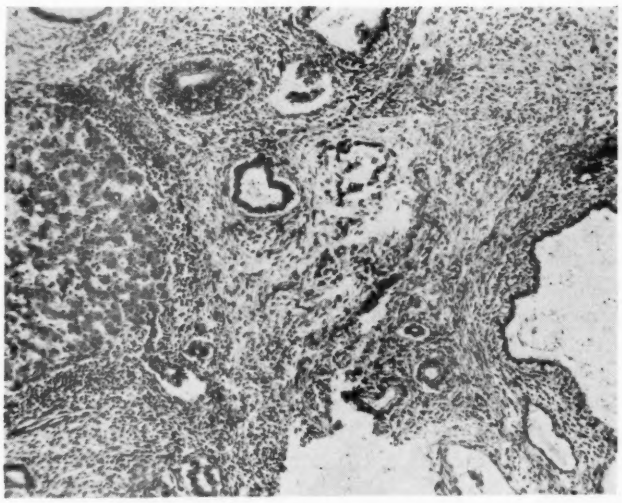


Fig. 9 (Case 9).—Baby Girl S. died one hour after birth. The presacral tumor was very large, weighing 640 grams in a 1,900 gram premature infant. Photomicrograph (×100). The island of obvious liver tissue in this section of the sacral tumor is an unusual finding. Elsewhere note the great variety of atypical epithelial structures in the usual curious stroma. (Photomicrograph reduced one-third.)

Microscopic sections showed glands of all sizes and shapes in a delicate connective tissue stroma. Some had columnar cells, others cuboidal. There were large masses of obvious liver tissue with Kupffer cells, and there were glands resembling pancreas. In another area was glial tissue with rows of round cells suggesting the molecular layer of the cerebellum. Masses of cartilage were present in another area. A glandlike structure with columnar epithelium lay near a bit of cartilage and mucus glands and suggested a bronchial structure. The skeletal muscle attached to the sacrum was invaded by the tumor.

Summary.—A 7-month premature white newborn infant girl died shortly after birth. Autopsy revealed massive sacral tumor, with evidences of local invasion of muscle and cartilage. Pressure upon the ureters had already produced hydroureter and marked hydronephrosis.

CASE 10.—E. K. (152065) was first seen at this hospital Oct. 3, 1915, for a sacral tumor. At that time she was 2 days old and had a 3 cm. swelling over the sacrum, firm and slightly moveable. The anus was displaced far forward and almost occluded.

Jan. 12, 1917, she was examined by Dr. Halsted, who considered the lesion to be a lymphangiomatous tumor of fetal origin and advised operation "in 6 months." Almost immediately infection in the tumor required incision and drainage. No biopsy was taken. From then until 1938, an interval of 23 years, the tumor drained constantly—thick jelly-like material, pus, and blood.

By 1938 the tumor measured 13 by 8.5 by 6 cm. projecting from the sacrum near the midline. Rectal examination was negative. The tumor was excised and a dense attachment found on the anterior aspect of the sacrum. The mass extended deep into the pelvis. The wound became infected and healed by secondary intention. The huge specimen was preserved intact at the time and sections were not made, but the description is clearly that of a presacral teratoma with a postsacral component.

Summary.—A large tumor of the sacral area grew steadily from the patient's birth until removal 23 years later. It was infected and drained blood, pus, and mucus for 21 years. Its jellylike contents, location, firm attachment to the anterior surface of the sacrum, and presence at birth all point to its being a presacral teratoma although microscopic studies were not made.

CASE 11.—L. L., a Negro male infant, was first seen in May, 1914, at the age of 3 months because of a large fluctuant tumor, "the size of a hen's egg," which had been noted at birth and was situated over the coccyx. The child was the second born to young and healthy parents, and the pregnancy and delivery had been normal. The tumor was not treated.

At the age of 1 year, the patient was admitted to the hospital because of pneumonia and a note was made that the tumor had grown only proportionately to the growth of the child. At that time the tumor was described as arising from the right buttock above the ischial tuberosity, being elongated and measuring 8 by 3 cm. It extended down to the anal orifice and entered the pelvis, where a large mass could be felt rectally. The consistency of the tumor was soft and fluctuant superiorly and rather cartilaginous inferiorly. No note was made of urinary or fecal obstruction.

Three months later, at the age of 15 months, the patient was seen again in the clinic and a note was made that the tumor was growing rapidly. The child died on July 14, 1915, at the age of 16 months. The death certificate gave uncomplicated pneumonia as cause of death, but it appears likely that the enlarging tumor at least played a part. No autopsy was performed.

Summary.—A Negro male infant died at 16 months of age. He had a sacral tumor, palpable rectally, present at birth. There had been recent rapid growth. Death occurred outside the hospital.

SUMMARY

Nine proved cases of presacral teratoma are reported. Presacral teratomas are large tumors, present at birth, arising between the sacrum and the rectum. It is likely that they arise in the fetus, where multipotent embryonic tissue escapes from the influence of forces normally responsible for coordination of growth or differentiation. The tumors may contain, in disordered and confused mélange, tissue suggestive of practically all the body organs and tissues but seldom with any degree of organization or the appearance of any adult organ.

The tumors usually present externally, but at times, as in Case 5, the tumor is inconspicuous externally until the occurrence of rapid growth or malignant changes. Death may result while the tumors are still benign from ulceration and infection, or from obstruction to rectum, urethra, or ureters. Malignant trans-

formation is relatively common and ordinarily it is a single cell type which becomes malignant, generally producing a papillary adenocarcinoma. Of our 9 proved cases there were 3 deaths from metastases from the malignant teratoma and one from massive local recurrence of an incompletely removed benign teratoma. Newborn infants tolerate removal of these large tumors quite well and immediate operation is required to forestall pressure symptoms or development of metastases.

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